American Journal of

PUBLIC HEALTH

and The Nation's Health

Prepared in Two Parts
Part 2

MEASURING the RISK of CORONARY HEART DISEASE in ADULT POPULATION GROUPS

A Symposium

volume 47
number 4

APRIL, 1957

These papers were presented before a Joint Session of the Epidemiology, Food and Nutrition, and Statistics Sections of the American Public Health Association at the Eighty-Fourth Annual Meeting in Atlantic City, N. J., November 15, 1956.

The publication of this symposium is supported by a grant from the National Heart Institute.

Supplement, April, 1957

MEASURING the RISK of CORONARY HEART DISEASE in ADULT POPULATION GROUPS

A Symposium

Measuring the Risk of Coronary Heart Disease in Adult Population Groups

I. The Cardiologist Enlists the Epidemiologist 1
PAUL DUDLEY WHITE, M.D.

II. Coronary Heart Disease in the Framingham Study 4
THOMAS R. DAWBER, M.D., FELIX E. MOORE, AND GEORGE V. MANN, M.D.

III. A Prospective Study of Degenerative Cardiovascular Disease in Albany: Report of Three Years' Experience—1. Ischemic Heart Disease . . 25
JOSEPH T. DOYLE, M.D.; A. SANDRA HESLIN; HERMAN E. HILLEBOE, M.D.; PAUL F. FORMEL; AND ROBERT F. KORNS, M.D.

IV. The Clinical Status of a Population Group in Los Angeles Under Observation for Two to Three Years 33
JOHN M. CHAPMAN, M.D., M.P.H.; L. S. GOERKE, M.D., M.S.P.H.; WILFRID DIXON, PH.D.; DONALD B. LOVELAND; AND EDWARD PHILLIPS, M.D.

V. An Epidemiological Investigation of Coronary Heart Disease in the California Health Survey Population 43
ROBERT M. DRAKE, M.D., M.P.H.; ROBERT W. BUECHLEY; AND LESTER BRESLOW, M.D., M.P.H.

Discussion:

Implications to the Biostatistician 58
ANTONIO CIOCCO, D.Sc.

Implications to the Nutritionist 60
NEVIN S. SCRIMSHAW, M.D.

Summary: 63
JAMES WATT, M.D.

I. The Cardiologist Enlists the Epidemiologist

PAUL DUDLEY WHITE, M.D.

I appreciate the opportunity as an internist primarily interested in cardiovascular disease, that is as a cardiologist of long standing, to take part in your public health program today. In introduction, I would like to emphasize the fact that I am primarily a practitioner of medicine, the son of a family doctor, and therefore, directly concerned with the individual patient who is the basis for all the important superstructures that have been added in the generations and decades that have passed, consisting of medical education, medical research, and public health. As one grows older in medicine, one naturally tries to unite the preventive aspects of health and disease to the care and advice one gives to one's private patients and their families. I spend a certain amount of time nowadays in advising fathers and mothers who are ill with heart disease about the future of the health of their children and of their childrens' children.

The most important kind of heart disease that has alarmed the world in general and this country in particular of late is, of course, coronary heart disease. During the last 35 years it has been the lot of cardiologists in the larger centers in America to face the growing threat of this scourge which began to be recognized as a possible danger to our civilization about ten years after James Herrick presented to us his memorable clinical discovery of coronary thrombosis itself. The first case of my own diagnosed as coronary thrombosis was in the second year of my private practice in January, 1921, and since that time I have seen increasingly every year a good many hundreds of cases. At first it was natural that our chief interest would be in the improvement of the diagnosis and treatment of the disease, but about 20 years ago attention began to be focused on a study of its causes. Prior to that time, there were only a few workers in this wilderness like Timothy Leary in Boston, Anitschkow in Moscow, and Aschoff in Germany, to present the needs for research.

Today we cardiologists realize the importance of enlisting the help of many experts in other fields in our attempts to solve the problem. These fields extend from the extreme of basic sciences —mathematics, physics, and chemistry— to the whole gamut of applied sciences— engineering, biology, comparative anatomy, physiology, and pathology. Experimental researches on animals in the laboratory, which should include much more study than now of the monkey, the application of physical and engineering laws, including hydrodynamics, to the effect on delicate tissues like the intima of the coronary arteries and aorta, and physiopathological effects of factors outside the artery walls and blood stream. All of these are in relatively early stages of research. Among the investigators must be included geneticists, of which we have far too few, and biostatisticians with whom the physicians themselves can work closely and in a practical way with mutual respect and cooperation. We must utilize the help of all these experts. This year happily, for the first time, funds have been allocated, both publicly and privately, to begin to study these problems

Dr. White is emeritus professor of medicine, Harvard University Medical School, Boston, Mass.

more adequately, and especially to train future investigators.

We practitioners know from our own experience that basic factors behind coronary heart disease are of very great importance. These include the possible influence of race, the sure influence of heredity, of sex and of age, and quite likely X factors that are basic but of which we have not even thought as yet. Inasmuch as at present we can do little or nothing in the control of these factors, namely of race, heredity, sex, and age, despite the possibility of future practical application of some eugenic principles, it is quite natural to believe that we should spend even more time in efforts to protect candidates for coronary heart disease, concerning whom we have acquired some information of late, by practical and sensible modifications of environmental factors and their ways of life.

Environmental factors include stress and strain, about which we know relatively little, exercise, which some of us believe important but just how and why we do not know, local customs and personal habits, for example, in the use of tobacco and alcohol, and proper programs of rest and relaxation, and diet. There are still other factors not adequately recognized or even known as yet which we might call Y factors, corresponding to the unknown basic X factors. Laboratory experiments on animals and clinical and laboratory studies on man have been done fruitfully and should be continued, but a much neglected field, the surface of which has barely been scratched during the last five or 10 years, is that of the relationship of the ways of life to heart disease which we have come to call epidemiological cardiovascular research.

A good many of us who have been interested in the study of the etiology of coronary heart disease, long before the professional epidemiologists themselves took up the cudgels, have asked for help in the solution of the problem through emphasis on the probable importance of environmental factors in the causation and aggravation of the disease. We have talked for years about the relationship of the ways of life to the development of coronary atherosclerosis; for example, in my Hermann Biggs Lecture in New York City in 1940, I suggested the value of comparing 1,000 Vermont farmers who were then working physically hard with 1,000 New York bankers who at that time were still affluent, but this proposal was mostly talk and was interrupted by the Second World War. It has been only in the last few years that some of us have ourselves gone actively into the field, meanwhile hoping to enlist those who previously had been especially trained in epidemiological methods which, of course, in the past have been used largely in the fields of infectious diseases and malnutrition. The day of united effort is now dawning and we cardiologists must take advantage of the experience and the skills of the professional epidemiologist, while he in turn must learn about cardiovascular disease and get from us our firsthand experience with this malady. The initial studies that have been made during the past few years by such pioneers as Ancel Keys will now have more adequate support and development in the future. We should meanwhile pay tribute in the over-all picture to the early workers for their very important preliminary studies. It is probable that work in the field itself will continue to be more fruitful in the long run than armchair philosophizing, important as it is to do careful preliminary planning. We must always take advantage of lessons learned in the field.

My own experience to date has been that important clues can come from individual intelligent patients as well as from mass studies. A single observation by a single person may actually be more important in the long run than hastily

drawn conclusions from inadequately analyzed series of thousands of persons. We must keep our feet on the ground from both standpoints and make use of the family doctor as well as of the public health departments throughout the world. The cooperation of the family doctors is now most encouraging. A recent visit to Grand Forks, N. D., has demonstrated this to me. At a breakfast conference on a Sunday morning, more than 100 of the 135 total medical community assembled to discuss their part in the survey of coronary heart disease in the six northeastern counties of that state, with fringes in Canada and western Minnesota in the Red River Valley. From a study such as this can come much fruitful information, especially when a comparison can be added between such people living in this community of rich farm land with others of the same race living under far different circumstances. This type of investigation is new, complicated, difficult, and expensive, but it must be done and with the greatest care. The various factors must all be weighed and, although diet and its details, for example the actual kinds of fat involved, are currently in the limelight, we must not forget the basic factors of which I have already spoken and other environmental factors such as exercise, stress and strain, and personal habits. "One man's meat is another man's poison" doubtless still holds true with respect to coronary atherosclerosis and its sequelae.

Finally, here is an opportunity for the establishment of international medical cooperation and friendship which can certainly advance the cause of world peace. Two years ago at the parting of a number of us from different countries, after an investigation in Naples, Italy, by a team including Swedes, Englishmen, an Australian, a South African, Italians, Americans, and a Yugoslav, a young Italian biochemist said in parting to his young Yugoslav colleague—"Isn't it strange that we were so recently at war?" The answer quickly came when the Yugoslav answered—"Why I never thought of it." I am quite sure that the furtherance of our program can do better than merely wishful thinking. The visit that some of us paid to Moscow in September, 1956, demonstrated clearly to us the desire of the physicians themselves and of public health workers to join us in the furthering of health and happiness throughout the world.

II. Coronary Heart Disease in the Framingham Study

THOMAS R. DAWBER, M.D.; FELIX E. MOORE, F.A.P.H.A.; and GEORGE V. MANN, M.D.

A continuing epidemiological study of heart disease was established in Framingham, Mass., during the period of 1948–1950. This study is concerned with measurements of the extent and development of cardiovascular disease in a cross-section of the population aged 30–59 on January 1, 1950, and with the study of those environmental and personal factors which are associated with the subsequent appearance and progression of cardiovascular diseases.[1] Data are obtained primarily from biennial examinations conducted in a clinic maintained especially for this study. It is planned to continue observation of the group of subjects for 20 years. The present report describes the experience with arteriosclerotic heart disease observed in the four years following each individual's initial examination.

Methods

A description of the town of Framingham and the methods by which the sample was drawn have been reported.[1] The response to this sample invitation was also discussed.[2] A summary of the cooperation obtained from the original sample in the first examination is shown in Table 1. The original health status and subsequent course of the persons who were selected, but not examined at the first examination, is the subject of continuing investigation, since this information has an important bearing on the generality of the findings of the study.

The original plan of the Framingham study provided for following only the persons in the sample who were free of arteriosclerotic heart diseast (ASHD) and hypertensive cardiovascular disease (HCVD). It was soon apparent that restriction of attention to this group, identified with difficulty at best, would result in the loss of much useful information concerning the life history of cardiovascular disease. Furthermore, it appeared that exclusion of diseased persons after the first examination would have weakened the clinic's relation with the community. For these reasons, persons with diagnoses of cardiovascular disease have been followed in this study along with those found free of this disease.

Table 1—Response to the Initial Examination

Response Status	No. of Persons	Per cent
Total sample	6,510	100
Examined	4,469	68.6
Not examined	2,041	31.4
Moved out of Framingham	421	6.5
Died before initial examination	74	1.1
Ill or incapacitated	74	1.1
Noncooperative	1,472	22.6

The organization of the clinic where the subjects were examined, the content of the examination, and the laboratory methods have also been described.[1] A detailed medical history and a physical examination was carried out by a physician. The findings of these procedures were entered on standard forms. Each

The authors are associated with the National Heart Institute, National Institutes of Health, Public Health Service, Bethesda, Md.

subject was seen by a second physician who evaluated the findings of the first. The laboratory examinations included measurements of vital capacity, height, and weight; an electrocardiogram; a standard chest film; measurement of hemoglobin, glucose, uric acid, cholesterol, and phospholipid; and serological test for syphilis. The protein, reducing material, and specific gravity were measured in the urine. Other procedures, such as 70 mm photofluorogram, electrokymography, ballistocardiography, and ultracentrifugal analysis of serum lipoproteins have been made at one or another of the successive examinations, but these have not been used for diagnostic classification. The chemical studies will be described in detail in another report.

At the completion of the examination the findings were briefly discussed with the subject and he was advised that he and the physician he had named would soon receive a report of the results of the procedure. The medical staff tried to avoid contributing medical advice or therapy beyond that necessary in situations of medical emergencies, e.g., breast tumors, signs of congestive failure, untreated diabetes, or unrecognized and acute evidence of coronary heart disease. The report sent the physician was analogous to a hospital discharge summary and listed the diagnoses established, but it did not contain recommendations for therapy. The research records were available to these physicians upon request. The subject was sent a form letter which said in effect, and as appropriate, "you were found to be free of cardiovascular disease," "we have confirmed the existence of a condition of which you were aware," or "we believe you should see your doctor concerning our findings." While it would be desirable from an epidemiological point of view to observe the occurrence of disease among individuals who were unaffected by knowledge of the observations this is not feasible, because the clinic physicians were obligated in some instances, by the urgency of the findings, to encourage the subject to place himself under the care of his physician.

Follow-Up Procedure

The subjects were examined with the same procedures on or near the biennial anniversary of their original examination. They were reached by telephone or mail and invited to accept an appointment. If a subject did not accept, the reason for the refusal was sought and recorded. The health status of each person who could not be reached directly was sought through relatives, neighbors, or associates. Every effort was made to determine whether the subject was living or dead. In this way the optimal information of an examination in the clinic was supplemented with less reliable information obtained through the subject's personal associates.

An analysis of the follow-up status of the 4,469 subjects who were initially examined is shown in Table 2. It is instructive to measure this follow-up performance for two kinds of sources of information, namely, "clinical" data for living subjects and "mortality" data for the others. This procedure is appropriate, since these sources are often of quite different reliability. The clinical information was obtained largely from the observation of subjects at their successive visits to the clinic, or from the records of nearby hospitals. The death data arose from the files of medical examiners, state and local health departments, and the clinical or autopsy reports of hospital deaths. During the early years of the study there were two general hospitals in the community. All the admissions of the subjects in the study to the larger (and presently the only) hospital in Framingham were reviewed in order to obtain data for those admitted for cardiovascular diseases.

Table 2—Completeness of Clinical and Mortality Follow-Up Four Years After Initial Examination

	No. of Persons	Per cent
Clinical Follow-Up		
Total sample	4,469	100
Persons with complete 4-year follow-up	3,984	89.1
Received examination III *	3,931	
Skipped examination III, but examined at IV	53	
Persons with 2-year clinical follow-up	193	4.3
Refused examination at III	113	
Moved before examination III	45	
Died before examination III	35	
No clinical follow-up	292	6.5
Refused examination at II and III	194	
Moved before examination II	60	
Died before examination II	38	
Mortality Follow-Up		
Total sample	4,469	100
Known dead in 4-year follow-up period	73	1.6
Known living at end of 4-year follow-up	4,349	97.3
Known living at 2 years, status unknown at 4 years	19	0.4
Follow-up status unknown	28	0.6

* The successive biennial examinations of the Framingham study are designated with Roman numerals, thus Examination III was 4 years after Examination I.

This information supplemented the history given by subjects who returned to the research clinic for examination, and it served as a reliable source of information on hospitalized disease developing in persons who did not return to the research clinic. Information concerning admissions to the second hospital, as for other surrounding hospitals, was not obtained for all sample persons in a systematic way, but was requested when the subject returned to the clinic and indicated that he had been admitted to a hospital with a disease known or suspected to be cardiovascular.

The data of Table 2 indicate that 89 per cent of persons initially examined who could have been followed were followed clinically for four years. An additional 4 per cent of the population were followed for two years. In terms of man-years of exposure, clinical data are available for 91 per cent of the years lived in the four-year, follow-up period. Mortality follow-up was much more complete. Only 1 per cent of the total sample could not be accounted for in respect to mortality status at the end of the four-year period and many persons in this group had been followed for two years.

Classification of Arteriosclerotic Heart Disease (ASHD)

The criteria used for the classification of arteriosclerotic heart disease followed those of the New York Association.[3] For the present purposes the following manifestations of ASHD are considered:

1. Myocardial infarction, with either or both historical and laboratory evidence that was suf-

ficient for all observers to make this diagnosis.

2. Angina pectoris, with sufficient symptoms to lead all observers to agree with this diagnosis.

3. Coronary occlusion. "Sudden death" attributed to coronary heart disease.

4. Myocardial fibrosis. Death, with either clinical evidence of progressive cardiac failure in the absence of apparent cause, or with autopsy evidence of myocardial fibrosis which could be attributed to atherosclerosis of the coronary arteries.

5. Myocardial infarction, possible, ECG evidence only. Persons without a history consistent with myocardial infarction, but presenting electrocardiographic evidence suggesting, but not conclusive of, myocardial infarction.*

"Arteriosclerosis of the aorta" is not included in the present consideration and there were no instances of "sclerosis of a valve," each of which is an anatomical diagnosis. The decision to include the subjects with "myocardial infarction, possible, ECG evidence only" was based upon the demonstration that the subsequent clinical courses of persons so classified at the initial examination were more often complicated by definite ASHD than were those of persons classified as "possible myocardial infarction by history" alone. The decision was also influenced by the greater objectivity of ECG evidence.

There were many subjects with questionable evidence of coronary heart disease including: (1) those subjects from whom a history suggestive of myocardial infarction was obtained, but without any supporting laboratory or clinical evidence, and (2) those subjects from whom a history suggestive of angina pectoris was obtained, in which the two observers were either in disagreement, or one or both were uncertain concerning the interpretation of these symptoms. These questionable manifestations of disease were grouped with other abnormalities, perhaps attributable to arteriosclerosis, such as generalized cardiac enlargement by x-ray, and left ventricular hypertrophy by ECG, or nonspecific abnormal T waves, each occurring in the absence of known causation. None of these is included in the category "arteriosclerotic heart disease" in this analysis. The relegation of these uncertain diagnoses to a less conspicuous category in the present analysis has an important influence upon the prevalence and incidence rates of ASHD. It seems clear that the final disposition of persons with these diagnoses of possible ASHD in a classification system cannot be solved until a long-term observation of their clinical implications has been made. Such an objective is a major concern of the Framingham study.

It should be understood that those persons with questionable evidence of ASHD at the first examination were, for purposes of incidence measurements, placed with all the other persons in the population. Neither those, nor many others in the population can be considered strictly normal people for, in addition to those with a question of ASHD, there were others with rheumatic heart disease (RHD), hypertensive cardiovascular disease (HCVD), and other diseases. These incidence estimates for a four-year period represent the rates of appearance of diagnosable ASHD in a population from which only those persons with definite ASHD have been excluded.

The classification of disease in subjects who died during the follow-up interval presents a different problem. The best available evidence concerning these subjects is derived from a hospital record of the terminal illness which may include an autopsy report. More often the information was only that included in a report of the medical examiner or

* The abnormalities observed were generally patterns of deep Q_3 and Q_{AVF} with or without inverted T wave which were considered to represent possible posterior infarction, and deep Q_1 with inverted T_1, usually with inverted T wave, in $V_{4,5,6}$ and with absent R waves over the right ventricle. The latter changes were consistent with a diagnosis of possible anterior infarction.

Table 3—Prevalence of Arteriosclerotic Heart Disease at the Initial Examination, by Age and Sex

Age	Males			Females		
	No. Examined	No. with ASHD	Rate/1,000	No. Examined	No. with ASHD	Rate/1,000
Total	2,024	48	24	2,445	28	11
30–44 *	1,083	5	5	1,317	7	5
30–34 *	335	2		389	1	
35–39	390	2		491	1	
40–44	358	1		437	5	
45–62	941	43	46	1,128	21	19
45–49	313	5		379	3	
50–54	319	18		365	8	
55–59	236	15		321	8	
60–62	73	5		63	2	

* Includes 5 males and 9 females aged 29 years; there was no ASHD among these people.

in the death certificate. Since ASHD is often a fatal disease, and particularly apt to end with "sudden death," the accurate etiological classification of these subjects constitutes one of the serious limitations of this and all similar studies of ASHD. The duration of the terminal illness is of critical importance in determining the extent of clinical evaluation and thus documentation of cause of death. The deaths which occurred in the sample population without sufficient clinical and laboratory evidence to permit a diagnosis of myocardial infarction, but which by their suddenness, the immediate appearance of the patient, and the exclusion of other probable causes lead the officials to conclude that this was caused by ASHD, have been called "coronary occlusion without myocardial infarction" in the present evaluation.

The tabulations shown represent an unduplicated count of persons. This was accomplished for subjects with more than one manifestation of ASHD by assigning a priority of importance to the various diagnostic categories. In diminishing rank this priority was

1. Myocardial infarction
2. Coronary occlusion without myocardial infarction
3. Angina pectoris
4. Myocardial infarction, possible, ECG evidence only
5. Myocardial fibrosis

In practice the application of this priority rule was not often necessary. One man who died suddenly has been classified as coronary occlusion, although he was known to have had angina pectoris. There were three persons classified as angina pectoris who also showed possible myocardial infarction by electrocardiographic evidence.

Results

Prevalence of Arteriosclerotic Heart Disease in 1949–1952 *

One product of the initial examination of the subjects in the sample population was an estimate of the prevalence of ASHD in the sample examined. These data are presented by sex and five-year

* Completion of the first cycle of examinations in the Framingham study required about four years.

Table 4—Number of Subjects by Type of Arteriosclerotic Heart Disease Diagnosed at Initial Examination, by Age and Sex

Diagnosis	Males			Females		
	Total	30–44	45–62	Total	30–44	45–62
Total	48	5	43	28	7	21
Myocardial infarction	17	2	15	1	–	1
Angina pectoris	20	2	18	18	5	13
Possible myocardial infarction, ECG evidence only	11	1	10	9	2	7

age interval in Table 3 for all diagnostic categories of ASHD combined. When the diagnoses are considered collectively the prevalence rates for the two sexes are very similar through age 49. In the sixth decade of life a remarkable increase in prevalence occurs in both sexes, but the increase is larger for men. The numbers of subjects over 59 years were too small to permit generalization about trend. It should be emphasized that these prevalence rates are based on counts of survivors of ASHD, as defined, who were able to attend the clinic, and the rates are, therefore, minimum estimates of the true prevalence.

In Table 4 these prevalence data are arranged by diagnostic category as well as by age and sex. Only the actual numbers of persons are shown, and thus the comparisons between diagnoses should be made only for specific age and sex groups. The most notable fact is the predominance of the diagnosis of angina pectoris in women in proportion to the total number of women with ASHD. Conversely, myocardial infarction was an uncommon disease in these women.

Table 5—Four-Year Incidence of Arteriosclerotic Heart Disease Among Persons Free of This Disease at Initial Examination, by Age and Sex

Age at Initial Examination	Males			Females		
	Population at Risk	New Disease	Rate/1,000	Population at Risk	New Disease	Rate/1,000
Total	1,976	65	33	2,417	32	13
30–44 *	1,078	13	12	1,310	–	–
30–34 *	333	3		388	–	
35–39	388	5		490	–	
40–44	357	5		432	–	
45–62	898	52	58	1,107	32	29
45–49	308	8		376	8	
50–54	301	15		357	8	
55–59	221	23		313	14	
60–62	68	6		61	2	

* Includes 5 males and 9 females aged 29 years; there was no new ASHD among these people.

Incidence of New ASHD in the Four-Year Follow-Up Interval

The four-year incidence of ASHD defined above as myocardial infarction, coronary occlusion, angina pectoris, myocardial fibrosis and possible myocardial infarction by ECG is shown by sex and age in Table 5. It should be emphasized again that the population at risk for this observation was composed of all the subjects in the sample except those with the diagnosis of ASHD at entry to the study as shown in Tables 3 and 4. The incidence rates were highly dependent on age and they were two to three times higher in males than in females. There is a suggestion that an upturn in the trend of incidence rates for each sex occurs at about age 45, a conclusion which has been used in grouping these data for subsequent analysis.

The incidence data are arranged by diagnosis for specific age and sex groups in Table 6. Since both fatalities and surviving persons are counted, it is of interest to consider the early mortality characteristics of ASHD. The prominence of "sudden death" as a manifestation of ASHD in men is a striking feature of these observations. Thirteen of the 43 men with "heart attacks" (i.e., myocardial infarction or coronary occlusion) were classified as "sudden death"; these persons, by the nature of the event, would not have reached the care and study of physicians. (This proportion for men aged 45–62 was 11 out of 31.) These data imply that studies of ASHD which are based upon autopsy material or hospital discharges are only partial observations of the disease. Angina pectoris, while almost as frequent a new manifestation of ASHD as myocardial infarction for men of all ages, occurred more commonly after age 45 than before. The data in Table 6 have been grouped into two age groups, 30–44 and 45–62 years. The older age group includes 80 per cent of all ASHD incidence for men and the entirety of the ASHD incidence in women.

The phenomenon of sudden death was the only manifestation of disease in almost half of all subjects with myocardial infarction who developed new ASHD exclusive of angina pectoris and possible myocardial infarction by ECG. In contrast to the sudden deaths are the so-called "silent" infarctions, the surviving subjects for whom the history of symptoms is absent or insufficient to contrib-

Table 6—Number of Subjects Developing New Disease in a Four-Year Period by Diagnosis and by Age and Sex

Diagnosis	Males			Females		
	Total	30–44	45–62	Total	30–44	45–62
Total	65	13	52	32	—	32
Myocardial infarction	30	10	20	4	—	4
Surviving persons *	27	9	18	3		3
Fatalities	3	1	2	1		1
Coronary occlusion w/o infarction †	13	2	11	1	—	1
Myocardial fibrosis with death	2	—	2	1	—	1
Angina pectoris	20	1	19	24	—	24
Possible myocardial infarction	—	—	—	2	—	2

* Survived to fourth anniversary of initial examination except for two persons who died from second coronary occlusion before Examination III.

† "Sudden death."

ute to the diagnosis, who were diagnosed on the basis of ECG evidence only. Seven of these "silent" infarctions occurred during the four-year follow-up period covered by this report, four among men and three among women. Indeed, one of these asymptomatic heart attacks was occurring (but was not diagnosed) at the time of the initial examination, since a second ECG made at a special examination one month later confirmed the usual evolution of ECG changes characteristic of a myocardial infarction. The total of seven of these asymptomatic or "silent" coronary attacks which occurred in the four-year follow-up period is to be compared with the total incidence of 36 persons with definite or possible myocardial infarction. The subject of "silent" infarctions has been discussed recently by Snow, Jones, and Daber [4] who concluded that the wide range of frequencies of this form of coronary disease was the result of the variable criteria applied in different studies. It is apparent that the "silent" coronary is an important part of the disease. Furthermore, there were persons in this study group who at some time showed definitive ECG evidence of a myocardial infarction but who later lost all residual evidence of ECG changes. The difficulty of diagnosing ASHD, underestimated by some,[5] will no doubt continue to obscure the evaluation of causal relationships.

Angina pectoris represents about one-third of all the new ASHD in men and this disease generally appeared in men after age 45. The new ASHD in women, occurring always after age 45, was predominantly angina pectoris. These data emphasize the dissimilarity of ASHD in the two sexes. The predominance of angina pectoris as the manifestation of ASHD in women suggests several possible explanations, none of which can be established with these data: (1) the diagnosis may be faulty. The greater prevalence of neurocirculatory asthenia in females [6] may lead to confusion with this disease, and (2) the manifestations of ASHD in women may differ from those in men. These problems may be resolved with additional observation. The tendency of the diagnosis of definite but uncomplicated angina pectoris in women to shift to questionable angina pectoris in successive examinations, and perhaps back to definite angina pectoris, suggests that the clinical interpretation of symptoms of angina pectoris in women is less reliable than in men. This shifting diagnosis was found despite rigorous attention to questioning technic and interpretative criteria. The variability must include, among other things, diagnostic error and the disappearance of symptoms of angina pectoris as a result of a decrease of physical activity or an adaptation to the symptoms. It will be necessary to trace the outcome of angina pectoris, the common manifestation of ASHD in women, in order to determine whether this condition is an antecedent stage of myocardial infarction and coronary occlusion, or whether the disease takes a different course in women.

The Association of Certain Clinical Attributes with the Development of ASHD

The Framingham study is predicated on the belief that an understanding of the pathogenesis of ASHD will be facilitated by a careful recording of the characteristics of the subjects before disease develops and analysis of antecedent differences between the group which develops disease while under observation and the group which does not. For the present analysis only the male subjects in the age range 45–62 at initial examination have been considered, since this is the only category in which new disease occurred with sufficient frequency in the first four years of follow-up to permit detailed analysis.

There were 52 men in this age group, free of disease at the initial examination, who developed ASHD in the subsequent four years; these represent 80 per cent of all men in the study who developed new ASHD in this follow-up period. The restriction of this analysis to the 45–62 age group was also influenced by the recognition that ASHD occurring before that age is relatively uncommon and possibly a different disease, since it is generally characterized by a more profound disturbance of cholesterol metabolism.[7, 8]

The analytical procedure in the following sections consists of the classification of individuals by various characteristics, such as blood pressure level, relative weight, or serum cholesterol level as these were observed at the initial examination. For each of these subgroupings of individuals who were at risk of coronary disease for the four-year follow-up, there is recorded the number of individuals who developed new disease and the incidence rate per 1,000 for the four-year period. It is then possible to test the null hypothesis that the observed differences between subgroupings are no greater than would be expected by chance variation of an incidence rate common to all subgroupings, given the numbers under observation. In the sections immediately following are shown data for blood pressure and hypertensive disease, relative fatness, and serum cholesterol which suggest that for each of these characteristics taken individually the assumption of no association appears untenable. In a subsequent section it will be shown that the three factors taken together will permit even stronger inferences as to association of these factors and risk of ASHD.

High Blood Pressure

It is widely believed that high blood pressure (HBP) augments the develop-

Table 7—Hypertension and Hypertensive Heart Disease in Relation to Incidence of ASHD in Four-Year Follow-Up, Males 45–62

	Population at Risk	New Disease	Rate/1,000
All persons	898	52	58
Definite hypertensive heart disease	82	8	98
Definite hypertension	124	10	81
Possible hypertensive heart disease	92	7	76
Borderline hypertension without heart disease	243	15	62
Normotension	310	8	26
(Cerebrovascular accident, or rheumatic heart disease not included above)	(47)	(4)	

Normotension: Left arm blood pressure determinations are below 140/90 on independent observations by two physicians.
Hypertension: Definite hypertension was diagnosed when both left arm systolic blood pressure determinations recorded by physicians were 160 mm Hg or over and/or all left arm diastolic blood pressures were 95 or over, or when each blood pressure reading was either a high systolic (160 or over) or a high diastolic (95 or over) level.
Borderline hypertension: All others.
Hypertensive heart disease: When in addition to definite hypertension, definite left ventricular hypertrophy or generalized cardiac enlargement by x-ray or left ventricular hypertrophy by ECG was present.
Possible hypertensive heart disease: When hypertension was definite in the presence of doubtful left ventricular hypertrophy (generalized cardiac enlargement) by x-ray or ECG or hypertension was doubtful, but with definite left ventricular hypertrophy or generalized cardiac enlargement or both hypertension and left ventricular hypertrophy (or generalized cardiac enlargement) were doubtful.

Table 8—Certain X-Ray and Electrocardiographic Findings in Relation to Incidence of ASHD in Four-Year Follow-Up, Males 45–62

	Population at Risk	New Disease	Rate/1,000
All persons	898	52	58
LVH or GCE by chest x-ray *	193	10	52
Definite	163	10	61
Possible	30	—	—
LVH or LV strain by electrocardiogram *	59	12	203
Definite	29	7	†
Possible	30	5	†

* These categories are not mutually exclusive.
† Rates not computed for base less than 50.

ment of ASHD. The prominence of this relationship has led some clinicians to conclude that the major part of the hypertension problem lies in the prevention of atherosclerosis. The relation of high blood pressure and hypertensive heart disease to the four-year incidence of ASHD in the Framingham study are shown in Table 7. The incidence rates indicate a trend from the low of 26 per 1,000 for 310 persons with normal blood pressure and free of all other kinds of heart disease to a high of 98 per 1,000 for 82 persons with definite hypertensive heart disease at the initial examination. It is clear that HBP is significantly associated with the incidence of ASHD ($X^2 = 10.2$, $n = 4$, $p = 0.04$).

The relationship of specific signs of hypertensive cardiovascular disease to the incidence of ASHD was considered. In Table 8 the relationship of cardiac hypertrophy measured with the chest film and with the ECG pattern of left ventricular hypertrophy (LVH) is considered. The x-ray diagnosis in this instance is based upon the radiologist's "pattern recognition" of generalized cardiac enlargement (GCE) and left ventricular hypertrophy. While this estimate is highly correlated with frontal area measurements of the heart and thorax which were also made, the latter have not been used in this evaluation. The data in Table 8 indicate that the x-ray diagnoses of definite or possible LVH or GCE were not associated with the development of ASHD. On the other hand, ECG evidence of LVH, whether definite or possible, was highly associated with the incidence of ASHD ($X^2 = 21.7$, $n = 1$, $p < 0.001$). These data raise many questions: Is the effect of HBP mediated through acceleration of atherogenesis, through precipitation of the occlusive event by mural damage which initiates thrombosis, or by myocardial hypertrophy which aggravates the inadequacy of coronary flow? The last proposal is not well supported by the low association of x-ray diagnoses of LVH and GCE with the incidence of new ASHD. The electrocardiographic diagnosis of LVH is, on the other hand, very highly associated with the incidence of new ASHD. It appears that these methods appraise different aspects of cardiac function. The explanation of this difference of association with the appearance of ASHD may lie in a lower sensitivity of this ECG pattern to cardiac damage. It is clear that this finding of LVH by ECG needs further study, because any laboratory measurement

which has predicted a fifth of the men who developed definite ASHD in four years may be adaptable to clinical needs.

Weight *

Since hypertension and obesity have been found to be correlated,[9] it is of interest to examine the relationship of some estimates of fatness and fattening to the incidence of ASHD. This task is complicated by the lack of either precise measurements of fatness or a definitive criterion for judging relative fatness. The actuarial data [10, 11] have tended to show that obesity, especially in men, is associated with a large increase in the risk of ASHD. These conclusions have been based upon very large, if superficially observed, populations with the assessments of obesity derived from weight and height measurements collected by many people under variable conditions. The criteria of obesity in most of those studies have been derived from the actuarial tables of observed weight for height and sex collected in the early part of this century. Because of the limitations of these methods it was elected to establish a reference base of weight by sex and height within the Framingham population.

The present analysis of the relation of weight to ASHD has been based on an index relating height to weight which, in order to prevent confusion with other relative weight indexes, will be termed "Framingham relative weight" (FRW). This index is the ratio (x 100) of an individual's observed weight to the median weight for his sex-height group in the entire Framingham cross-section at the initial examination. The median weights are, thus, based on a population with an age range 29–62 with the distribution of ages shown in Table 3. Medians were computed for the male population for each inch of height in the range 61–73 inches. In this range there was clearly a linear relation between median weight and height and the data were smoothed by use of the following formula (where weight is in pounds and height in inches): Median weight $= 136 + 4$ (ht. -60).

An extrapolation of one inch was made in each direction to cover the height range 60–74 inches which included all but five of the men aged 45 or over. Since obesity is common in this population, it follows that the weight distributions reflect this in the parameters; but the ratio of an individual's observed weight to the median weight for height of the population, which is called the "Framingham relative weight" (FRW), does not presume to judge desirability, only to supply a reasonably stable denominator or reference base for the individual's observed weight.

The data presented in Table 9 support the hypothesis that obesity is related to risk of coronary attack ($X^2 = 12.8$, $n = 3$, $p = 0.005$). The upper tenth of the population in respect to "Framingham relative weight" showed an incidence rate three times that of the population whose weight was below the median for height. There was a regular downward progression of incidence rates from the highest relative weight group down to the median; with the small amount of data at hand there appeared to be no gradient in the group below the median.

The study also provided information on change of weight since age 25 based on the subject's recollection of his weight at that age. Although this kind of information is liable to considerable memory error, it may be a useful alternative way of estimating obesity, if a man's weight at 25 is considered in some sense his "ideal weight." The association of this

* Men were weighed and measured with shirt and shoes removed. Height was recorded to next lower quarter inch and weight to the next lower quarter pound. Tabulations were made on data coded to the next lower full inch and the next lower full pound.

Table 9—Framingham Relative Weight and Weight Changes Since Age 25 in Relation to Incidence of ASHD in Four-Year Follow-Up, Males 45–62

	Population at Risk	New Disease	Rate/1,000
Framingham relative weight:			
All persons	898	52	58
120 or more	81	10	123
113–119	95	10 *	105
100–112	320	16 *	50
Less than 100	397	16	40
Unknown	5	—	—
Weight change since age 25:			
All persons	898	52	58
Increase 30 per cent or more	78	9	115
Increase 20–29 per cent	123	12	98
Increase less than 20 per cent	572	24	42
Unknown	125	7	56

* Two persons with new disease, outside of height range for which relative weights were regularly computed have relative weights computed by extrapolation as follows: (1) 56 inches, 121 lbs., extrapolated FRW, 100; (2) 58 inches, 140 lbs., extrapolated FRW, 116.

measure with the present Framingham relative weight for individuals is high. Increase of weight since age 25 is associated with increased risk of coronary disease ($X^2 = 10.9$, $n = 2$, $p = 0.005$). These data on weight are confirmatory of life insurance studies, but are in contrast with the findings described by Keys [5] who found that only 4.8 per cent of a group of 105 men with "ischemic heart disease" were above a relative weight of 120 using a distribution of relative weight not markedly different than that used here. In the present experience, of 52 men with ASHD, 10 (19 per cent) were in the group with relative weight exceeding 120.

The present experience confirms the widespread belief that obesity is associated with the development of ASHD. The observed incidence rate in men with FRW of 120 or more was about twice that of the entire population and three times that of men with FRW less than 100. However, there is little or no relation of moderate obesity with new ASHD. Since only 10 per cent of the Framingham population falls above the FRW of 120, it follows that these are very obese people. For example, the FRW of 120 for a man 68 inches tall would be 202 pounds.

Serum Cholesterol

A number of studies have shown the association of elevation of serum cholesterol with increased incidence of arteriosclerotic heart disease. The recent, nation-wide Cooperative Lipoprotein Study included data on serum samples supplied by the Framingham study, although those cholesterol determinations were carried out in another laboratory.[8] The data presented here are based on determinations of serum total cholesterol which were made in the Framingham laboratory by the method of Abell, et al.[12] During the period when much of the data were being collected the laboratory standardized its results by exchange of serum samples with the four

Table 10—Serum Total Cholesterol in Relation to Incidence of ASHD in Four-Year Follow-Up, Males 45–62

	Population at Risk	New Disease	Rate/1,000
All persons	898	52	58
Cholesterol measured at Examinations I or II:			
260 mg per cent and over	172	21	122
225–259 mg per cent	265	12	45
Less than 225 mg per cent	445	18	40
Unknown	16	1	*
Cholesterol measured at Examination I: †			
260 mg per cent and over	131	16	122
225–259 mg per cent	188	8	42
Less than 225 mg per cent	334	13	39
Unknown	228	14	61

* Rate not computed for base less than 50.
† Included above.

laboratories participating in the Cooperative Lipoprotein Study.

Cholesterol determinations were not made during the early stages of the program, and as a consequence 228 of the 898 men in the age group under study did not have a value recorded at the time of the first examination. All but 16 of the 228 did, however, have a cholesterol value recorded at their second examination, and that value has been used for classifying those men. As a result, seven of 51 new events occurred in men prior to the recording of a cholesterol value; one man died before the second anniversary of his initial examination and is not represented in the series. In Table 10 the data are presented in two ways: first, based on the first cholesterol value recorded for each man, whether it was measured at Examination I or Examination II; and the second, showing results using only data recorded at Examination I. It will be noted that the same conclusions would be reached using either body of data.

There is an increased risk of ASHD in persons with elevated cholesterol levels ($X^2 = 16.2$, $n = 2$, $p < 0.001$), but no apparent gradient below a level of 260 mg per cent. The division at 260 mg per cent is an arbitrary one and well above the mean level of 225.5 mg per cent found for the entire group of Framingham men in this age range.

The Interaction of High Blood Pressure, Obesity, and Hypercholesteremia with Respect to Risk of ASHD

The data in the preceding section indicated that hypertension, obesity, and hypercholesteremia were each associated with increased risk of ASHD in a group of men 45–62. In this section it will be shown that these attributes appear to make independent but varying contributions to risk, and the joint elevation of two or three is associated with a greatly increased risk.

In this group of men the three attributes are not highly interrelated. As shown in Table 11, the correlation between blood pressure and relative weight

Table 11—Intercorrelations of Blood Pressure, Relative Weight, and Total Cholesterol, Males 45–62

Attributes			Product—Moment Coefficient of Correlation *
Systolic pressure	x	relative weight	0.27
Diastolic pressure	x	relative weight	0.33
Systolic pressure	x	cholesterol	0.09
Diastolic pressure	x	cholesterol	0.12
Relative weight	x	cholesterol	0.06

* $n = 877$, $\sigma_r \cong 0.034$.

is low, and there is almost no correlation in this age group between serum cholesterol level and either blood pressure or relative weight. It is important to consider the independent contribution that each of these attributes makes to the risk of developing ASHD, because each of them is more or less susceptible to individual study and control.

The data in Table 12 show the extent to which high blood pressure, high relative weight, and high serum cholesterol levels are associated with increased risk of coronary disease when elevation of any one is found in a man who has

Table 12—Incidence of ASHD in Four-Year Follow-Up, Males 45–62 Classified According to Level of Blood Pressure, Relative Weight or Cholesterol Level (Effect of Other Variables Partly Controlled)

Attributes *			Population at Risk	New Disease	Rate/1,000
Blood Pressure	Relative Weight	Total Cholesterol			
All persons †			877	51	58
Classified on blood pressure (men with high relative weight or high cholesterol omitted):					
High	Med. or low	Med. or low	91	9	100
Borderline	Med. or low	Med. or low	242	9	37
Normotension	Med. or low	Med. or low	240	4	17
Classified on relative weight (men with high blood pressure or high cholesterol omitted):					
Border. or normo.	High	Med. or low	87	5	57
Border. or normo.	Medium	Med. or low	198	5	25
Border. or normo.	Low	Med. or low	284	8	28
Classified on cholesterol (men with high blood pressure or high relative weight omitted):					
Border. or normo.	Med. or low	High	112	9	80
Border. or normo.	Med. or low	Medium	178	9	51
Border. or normo.	Med. or low	Low	304	4	13

* Classification of attributes:
Blood pressure
High—consistently 160 systolic or over or 100 diastolic or over
Normotension—consistently below 140 systolic and 90 diastolic
Borderline high blood pressure—all other
Relative weight
High—Framingham relative weight 113 or over
Medium—Framingham relative weight 100–112
Low—Framingham relative weight under 100
Total cholesterol
High—260 mg per cent or over
Medium 225–259 mg per cent
Low—under 225 mg per cent

† Excludes 21 persons for (one developing new disease) whom measurements of one or more attributes were not available.

Table 13—Incidence of ASHD in Four-Year Follow-Up, Males 45–62 Classified According to Various Combinations of Blood Pressure, Relative Weight, and Cholesterol Levels

Attributes *			Population at Risk		New Disease	Rate/1,000
Blood Pressure	Relative Weight	Total Cholesterol	No.	Per cent		
All persons †			877	100	51	58
High on two or more			105	12	15	143
High	High	High	17		5	
High	High	Med. or low	47		3	
High	Med. or low	High	20		1	
Border. or normo.	High	High	21		6	
High on one only			290	33	23	79
High	Med. or low	Med. or low	91		9	
Border. or normo.	High	Med. or low	87		5	
Border. or normo.	Med. or low	High	112		9	
Border or medium on two or more			186	21	7	38
Borderline	Medium	Medium	48		4	
Borderline	Medium	Low	63		–	
Borderline	Low	Medium	42		3	
Normotension	Medium	Medium	33		–	
Border or medium on one only			198	23	5	25
Borderline	Low	Low	89		2	
Normotension	Medium	Low	54		1	
Normotension	Low	Medium	55		2	
Normotension or low			98	11	1	10
Normotension	Low	Low				

* See footnote on Table 12 for definition of attributes.

† Excludes 21 persons (one developing new disease) for whom measurements of one or more attributes were not available.

medium or low levels of the other two.* It will be seen that blood pressure level is clearly associated with risk of coronary disease in the absence of elevation of relative weight or cholesterol ($X^2 = 12.1$, $n = 2$, $p = 0.002$). The risk among men with high blood pressure who were in medium or low categories of the other two variables was about six times that of normotensive men. Cholesterol also showed a clear association with risk ($X^2 = 11.6$, $n = 2$, $p = 0.003$), and again the risk among men high in cholesterol was about six times that among men in the low group in the absence of elevation of blood pressure or relative weight. Although there is an indicated excess risk among men with high relative weight, on the data at hand the observed difference is not statistically significant ($X^2 = 2.3$, $n = 2$, $p = 0.32$). Apparently most of the association of risk of coronary disease with obesity is accounted for by the

* For this and the following analysis the level of blood pressure which is termed "high" is different from the definition of "hypertension" used in Table 7. "High blood pressure" is defined here as pressure consistently at or above 160 mm Hg systolic or 100 mm Hg diastolic. Use of this criterion places 20 per cent of the men in the "high" category and thus corresponds to the relative weight criterion of 113 and the serum cholesterol criterion of 260 mg per cent, each of which place 20 per cent of the men in the "high" category.

Table 14—Incidence of ASHD in Four-Year Follow-Up, Males 45–62 Classified According to Blood Pressure and Cholesterol Levels

Attributes *		Population at Risk		New Disease	Rate/1,000
Blood Pressure	Total Cholesterol	No.	Per cent		
All persons †		877	100	51	58
High on both		37	4.2	6	162
High	High				
High on one only		271	30.9	27	100
High	Medium	51		3	
High	Low	87		9	
Borderline	High	75		10	
Normotension	High	58		5	
Border or medium on both		115	13.1	8	70
Borderline	Medium				
Border or medium on one only		284	32.4	8	28
Borderline	Low	187		6	
Normotension	Medium	97		2	
Normotension or low		170	19.4	2	12
Normotension	Low				

* See footnote on Table 12 for definition of attributes.

† Excludes 21 persons (one developing new disease) for whom measurements of one or more attributes were not available.

association of obesity with high blood pressure.

In Table 13 all three attributes are considered simultaneously. There is an evident association of these groupings with risk of ASHD ($X^2 = 25$, $n = 4$, $p < 0.001$). Consider first the bottom group which includes the 11 per cent of the men 45–62 who were characterized by low values in all three variables, i.e., blood pressure less than 140/90, FRW less than 100, and cholesterol less than 225 mg per cent. The incidence rate for this group was 10 per 1,000, a rate even lower than that observed among all women of the same age (29 per 1,000). The presence of borderline or medium levels of one or more of the three attributes is associated with progressively increased risk. Definite elevation of any one of the three is associated with a markedly increased risk—79 per 1,000. The concomitant elevation of two or more variables is associated with an indicated four-year incidence of 143 per 1,000. It is thus possible to contrast a small group (one-eighth of the men) who have an indicated risk of one in nine of developing recognizable ASHD in four years with a similarly sized group at the opposite end of the scale who had an indicated risk of one in 100. In view of the small number of new events on which this analysis is based it is perhaps more appropriate to compare the experience of the men in the two upper groups with that of the men in the two bottom groups. The two upper groups, which include the 45 per cent of the men high on any one of the three attributes, have an incidence rate of 96 per 1,000 and include 75 per cent of the men who developed disease. The two bottom groups which include 34 per cent of the men have an incidence rate of only 20 per

1,000 and include only 12 per cent of the men who developed disease. Of particular interest are the 17 men who were high in all three attributes. In this group there were five new occurrences—odds of five to 12 to lose in four years.

In view of the suggestion that the effect of obesity on risk may be through its relation with hypertension data are presented in Table 14 classified on blood pressure and cholesterol only. It is possible using only these two variables to separate out a group high on one or the other of the two which includes 35 per cent of the men and two-thirds of the new disease (33 out of 51). The four-year incidence in this group was 107 per 1,000. This group may be contrasted with a group of men who were low on both, or medium or borderline on only one, which included over half of the population (52 per cent), but only 20 per cent of the new disease (10 out of 51). The four-year incidence in this "low" group was 22 per 1,000—only one-fifth of the incidence found in the high group.

Education

The formal educational experience of the subjects in the Framingham study may be used as an index of the relationship of socioeconomic status to the risk of developing ASHD (Table 15). Although the incidence rate of 70 per 1,000 for persons with no more than grade school education is slightly higher than that of the base population, it does not prove to be significantly higher, and the absence of a trend among the other categories gives no suggestion of an important association. It is of interest that men with high school, college, business, or graduate school training showed rates no greater than those with less education. There is very little evidence in these data to suggest a relationship of socioeconomic status with the appearance of ASHD, although the classification by education may not be a sufficient index of this variable. Since the Framingham population contains an unusually broad array of occupations, this attribute will be studied in greater detail. Morris [13] also found but little relationship between educational accomplishment and the risk of coronary disease in the British occupational mortality experience.

Smoking

It has been proposed that smoking is associated in varying degrees with the development of ASHD.[14, 15] The data in Table 16 illustrate certain interpreta-

Table 15—Education in Relation to Incidence of ASHD in Four-Year Follow-Up, Males 45–62

Educational Status	Population at Risk	New Disease	Rate/1,000
All persons	898	52	58
Grade school only, or none	386	27	70
High school, not graduated	139	6	43
High school graduate *	182	9	49
College	158	8	51
Unknown	33	2	†

* Includes "business college" and specialized trade school subsequent to high school graduation.
† Rate not computed for base less than 50.

Table 16—Smoking Pattern Recorded at Initial Examination and Incidence of ASHD in Four-Year Follow-Up, Males 45–62

Smoking Pattern	Population at Risk	New Disease	Rate/1,000	
All persons	898	52	58	
Never smoked	107	9	84	70
Lapsed	78	4	51	
Cigar or pipe only	131	5	38	36
Cigarettes per day:				
Less than 10	91	3	33	
10–15	76	7	92	
20	204	14	69	72
25–35	79	3	38	
40 or more	55	6	109	
Unknown	77	1	13	

tive difficulties in the present body of data. The variability of attack rates is large and without a regular progression among men with different smoking habits. Any attempt to consolidate persons into broader categories of smoking habits in order to gain the advantage of larger numbers has major effects upon the resultant incidence rates. Nevertheless, very heavy smokers showed high incidence and the light cigarette smokers and pipe and cigar smokers showed lower incidence of ASHD. But persons who had never smoked, or had quit smoking, showed a rate as high as the entire group who reported smoking 10 or more cigarettes per day. Doll and Hill,[16] in their second report on mortality among British doctors, showed an upward trend of mortality from coronary thrombosis in relation to smoking in men who were either under 55 years or 75 and over, but very little trend in the age range 55–74. Generalizations cannot be made until additional morbidity and mortality experience become available from the present study, but these data do suggest that the association of ASHD with smoking is not as strong as that shown with elevated blood pressure, relative weight, and cholesterol.

Discussion

This study has identified three readily measured characteristics of human subjects which are frequently present in advance of the development of definite ASHD. These are high blood pressure, overweight, and hypercholesteremia. Each of these appears to have association with the development of the disease; the group of individuals in which all three are coincidentally high show great increases of incidence of ASHD. High blood pressure and hypercholesteremia in this group clearly have some independent association with risk of disease. The role of obesity, which is also associated with heart disease, is not as clear in view of the demonstrated association of high blood pressure and obesity. The demonstration of the association of these clinical attributes with ASHD should encourage the search for common factors and explanatory mecha-

nisms. This search should be a prime function of epidemiological studies of heart disease.

The extent that these findings can be used for generalization about the biology of ASHD is limited by the small experience with de novo disease, the possible bias introduced by the persons drawn in the sample who either refused original examination or were soon lost to follow-up, and finally by the imprecision of the diagnostic procedures. The first limitation will ultimately be met with additional follow-up. The principal evidence concerning the question of sample refusal is supplied by comparison of the mortality experience of the original participants and the nonparticipants. While mortality of the latter was excessive for a few years it is now reassuringly similar to that of the participants, and it does not appear to be a source of significant bias. The diagnosis of ASHD is extraordinarily difficult. These data have demonstrated that almost a third of subjects experiencing "heart attacks" die suddenly so that there is little or no opportunity to apply clinical and laboratory studies for the identification of the kind of antecedent disease. Another group, perhaps a fifth, have either no symptoms or trivial symptoms of heart disease, and yet show definitive evidence of new coronary artery disease in routinely obtained electrocardiograms. This difficulty of diagnosis compounds the uncertainty of studying atherogenesis by means of the clinical manifestation of ASHD. Nevertheless, since this clinical approach will probably remain the only feasible one, it is of first importance that some uniformity of criteria for the grouping of the clinical manifestation of ASHD be adapted in epidemiological studies.

Summary

1. An evaluation has been made of the prevalence of arteriosclerotic heart disease (ASHD) in Framingham, Mass., and the incidence in persons presumably free of ASHD in four years of follow-up.

2. The initial examination included 68.6 per cent of a randomly selected cross-section of the population aged 30–59 in 1950. Subsequent biennial examinations have obtained clinical information on 89.1 per cent of the initially examined population. Mortality information is available for 99 per cent of this population.

3. A working classification of ASHD has been adopted which includes myocardial infarction, coronary occlusion (sudden death attributed to coronary heart disease), angina pectoris, myocardial fibrosis, and possible myocardial infarction diagnosed by electrocardiographic evidence only.

4. ASHD was about twice as prevalent in men as in women at the first examination, and in men was comprised about equally of AP and MI. ASHD was uncommon in either sex under age 40.

5. There were 97 persons free of definite ASHD at the first examination who developed the disease in the subsequent four years of observation. The incidence rate for men was twice that for women.

6. All this new disease occurred after age 45 in women and 80 per cent after this age in men.

7. Almost half the men developing heart attacks died, and almost one-third of the men died suddenly.

8. About one-fifth of the new myocardial infarctions were asymptomatic.

9. The ASHD appearing in women was predominantly angina pectoris.

10. Among men 45–62 the presence of high blood pressure and HCVD was strongly associated with the development of new ASHD.

11. A reference table of weight for height was established for males and it was shown that fatness is associated with the development of ASHD in men 45–62.

Much of this association appeared to be explained by the association of obesity with high blood pressure.

12. Hypercholesteremia was strongly associated with the development of new ASHD in men 45–62.

13. The use of three factors in combination—blood pressure, relative weight, and serum cholesterol permitted the separation of men 45–62 into groups with highly divergent risks of ASHD. Classification on blood pressure and cholesterol without regard to relative weight also made possible separation into groups with large differences in risk.

14. Neither smoking habits nor educational background were notably associated with the development of new ASHD.

REFERENCES

1. Dawber, T. R.; Meadors, G. F.; and Moore, F. E. Epidemiological Approaches to Heart Disease: The Framingham Study. A.J.P.H. 41:279–286 (Mar.), 1951.
2. Dawber, T. R., and Moore, F. E. Longitudinal Study of Heart Disease in Framingham, Massachusetts: An Interim Report. In "Research in Public Health." New York: Milbank Memorial Fund, 1952.
3. Criteria Committee of the N. Y. Heart Association. Nomenclature and Criteria for Diagnosis of Diseases of the Heart and Blood Vessels. New York: New York Heart Association, 1953.
4. Snow, P. J. D.; Jones, A.M.; and Daber, K. S. A Clinico-pathological Study of Coronary Disease. Brit. Heart J. 18:435–441 (Oct.), 1956.
5. Keys, A. The Diet and Development of Coronary Heart Disease. J. Chronic. Dis. 4:364–380 (Oct.), 1956.
6. Kannel, W. B.; Dawber, T. R.; and Cohen, M. E. The Electrocardiogram in Neurocirculatory Asthenia. (In preparation.)
7. Lawry, E. Y.; Mann, G. V.; Peterson, A.; Wysocki, A. P.; O'Connell, R.; and Stare, F. J. Cholesterol and Beta Lipoproteins in the Sera of Americans—Well and With Coronary Heart Disease. Am. J. Med. (In press.)
8. Technical Group, Committee on Lipoproteins and Atherosclerosis of the National Advisory Heart Council. An Evaluation of Serum Lipoprotein and Cholesterol Measurements as Predictors of Clinical Complications of Atherosclerosis: A Report of a Cooperative Study of Lipoproteins and Atherosclerosis. Circulation 14:691–741 (Oct.), 1956.
9. Levy, R. L.; White, P. D.; Stroud, W. D.; and Hillman, C. C. Overweight: Its Prognostic Significance in Relation to Hypertension and Cardiovascular-Renal Disease. J.A.M.A. 131:951–955 (July 20), 1946.
10. Armstrong, D. B.; Dublin, L. I.; Wheatley, G.; and Marks, H. H. Obesity and Its Relation to Health. J.A.M.A. 147:1007–1014 (Nov. 10), 1951.
11. Dublin, L. I.; and Marks, H. H. Mortality Among Insured Overweights in Recent Years. Trans. A. Life Insur. M. Dir. Amer. 35:235, 1952.
12. Abell, L.; Levy, B.; Brodie, B.; and Kendall, F. A Simplified Method for the Estimation of Total Cholesterol in Serum and the Demonstration of Its Specificity. J. Biol. Chem. 195:357–366 (Mar.), 1952.
13. Morris, J. N. Coronary Heart Disease in 1950 with Some Related Observations. Brit. J. Indust. Med. 13:287–290 (Oct.), 1956.
14. Hammond, E. C., and Horn, D. The Relation Between Human Smoking Habits and Death Rates. J.A.M.A. 155:1316–1328 (Aug. 7), 1954.
15. Doll, R., and Hill, A. B. The Mortality of Doctors in Relation to Their Smoking Habits. Brit. M. J. 1:1451–1455 (June 26), 1954.
16. Doll, R., and Hill, A. B. Lung Cancer and Other Causes of Death in Relation to Smoking. Brit. M. J. 2:1071–1081 (Nov. 10), 1956.

ACKNOWLEDGMENTS—The Framingham study involves the efforts of a large number of specialists. The following have made important contributions to the success of the study over the period 1948–1956 which the authors wish to acknowledge.

The several thousand men and women of Framingham who have participated and:

Staff Physicians
Douglas Bragdon, M.D.
Susan Butler, M.D.
George Cytroen, M.D.
Buford Hall, M.D.
Abraham Kagan, M.D.
William B. Kannel, M.D.
Donald E. Love, M.D.
Gilcin F. Meadors, M.D.
David Miller, M.D.
Harold L. Osher, M.D.
Henry H. D. Sterrett, Jr., M.D.
Thomas Stevenson, M.D.
Joseph Stokes, III, M.D.
Richard B. Streeper, M.D.
Carlyle F. Stout, M.D.
John Vander, M.D.

Consultants
Joseph Benotti
Norbert Benotti
Bert Boone, M.D.
Mandel E. Cohen, M.D.
Laurence B. Ellis, M.D.
Lloyd E. Hawes, M.D.
Harold Levine, M.D.
Sylvester McGinn, M.D.
Lawrence Robbins, M.D.
Roger W. Robinson, M.D.
David D. Rutstein, M.D.
Conger Williams, M.D.
Stanley M. Wyman, M.D.

Nurses
- Marie Blaisdell
- Constance Elliot
- Aline Pournelle
- Mary Sullivan

Laboratory and Technical Personnel
- Norma T. Buscone
- William Claffey
- Arthur DeTore
- Janet Hill
- Rosemary Libby
- Albina Mariano
- Arline M. Mitchell
- Frederick Uhrig
- Marie Zock

Statistical Personnel
- Mary Ann Halperin
- Harold Kahn
- Irene Lima
- Dorothea M. McElholm
- Patricia McNamara
- Philip Person

Other Personnel
- Marquerite Dragon
- Mary Howes
- George Kenny
- Lorna Lyell
- Nell McKeever
- Leona Paris
- Anna Simonetta

III. A Prospective Study of Degenerative Cardiovascular Disease in Albany: Report of Three Years' Experience—I. Ischemic Heart Disease

JOSEPH T. DOYLE, M.D.; A. SANDRA HESLIN; HERMAN E. HILLEBOE, M.D., F.A.P.H.A.; PAUL F. FORMEL; and ROBERT F. KORNS, M.D., F.A.P.H.A.

Early in 1953 the New York State Department of Health in contract with the Albany Medical College established the Cardiovascular Health Center.[1, 2] The primary objective of the Center was to detect the earliest manifestations of degenerative cardiovascular disease in an especially susceptible population. Voluntary participation in this study was solicited of male New York State Civil Service employees 39 through 55 years of age residing in the Albany area. This is a stable, intelligent, and cooperative group, almost exclusively white and of predominantly Northern European extraction with large Jewish and Italo-American minorities.

Methods

At the first examination a detailed medical history was obtained, based on a comprehensive, self-administered questionnaire supplemented by an interview with a physician. A complete physical examination was done. The laboratory studies included the measurement of the hemoglobin concentration and of the serum total cholesterol level,[3] a urinalysis; 14 by 17 inch roentgenograms of the heart and lungs in the postero-anterior and lateral projections during cardiac systole; skinfold measurements at standardized sites[4]; a 12-lead electrocardiogram; and a high-frequency (Starr) ballistocardiogram.[5] Unless physically impossible or contraindicated by a history strongly suggestive of ischemic heart disease, all participants were subjected to a stress test, after which selected electrocardiographic leads and the ballistocardiogram were repeated. The first 715 men examined performed a master double two-step test.[6] All subsequent stress tests have consisted of a 10-minute walk at three miles per hour against a 5 per cent grade on a motor-driven treadmill.

An interval history, based on a short self-administered questionnaire and supplemented by a physician interview, was obtained for the second and third examinations. A complete physical examination was again done. The same battery of laboratory tests was done with one exception. Because of the accelerated schedule of examinations it was possible to perform stress tests on only half of the eligible participants at the second examination, and on the other half at the third examination. Numerous specialized studies have been carried out incidental to the reexaminations, some of which will be reported later.

Diagnostic Criteria

The term ischemic heart disease has been used in preference to coronary artery disease, not only because it has no etiologic or pathogenetic implica-

The authors are associated with the Cardiovascular Health Center and Department of Medicine, Albany Medical College, and the New York State Department of Health, Albany, N. Y.

Table 1—Follow-Up of Initial Study Group After 31 Months' Observation (Cardiovascular Health Center)

Age	Total Eligible Population	Examined At		Lost		
		I	III	Total	I–II	II–III
Total	2,202	1,913	1,682	231	156	75
Under 40	89	84	76	8	5	3
40–44	760	665	605	60	41	19
45–49	775	675	591	84	55	29
50–54	567	481	406	75	53	22
55 and over	11	8	4	4	2	2

tions, but also because it is semantically more precise. The diagnosis of ischemic heart disease has been based on: (a) an unequivocal history, preferably supplemented by medical records and electrocardiograms, of an acute myocardial infarction or, uncommonly, the electrocardiographic stigmata of a healed myocardial infarction without an appropriate history; (b) classical Heberden's angina; (c) an abnormal electrocardiographic response to exercise. The criteria of an abnormal electrocardiographic response to exercise have been: (a) depression of J (the RS-T junction) of 1.0 mm or more in the axial and of 1.5 mm or more in the lateral precordial leads; (b) coving of ST segments; (c) frank inversion of T_I or of T waves in the lateral precordial leads. These empirical criteria have evolved from experience and coincide closely with those employed by Mattingly and Robb.[8] The nomenclature of the New York Heart Association with minor modifications has been used in formulating cardiac diagnoses.[9]

Results

From February, 1953, through September, 1954, 1,913 men were examined, 89 per cent of those eligible. At the completion of the first reexamination in September, 1955, 156 participants had been lost, of whom 102 refused to return; 45 had left state employment and for various reasons found it inconvenient to return; and nine had died. In September, 1956, at the completion of the second reexamination 1,670 individuals had returned and 75 had been lost. Of these 75 men, 42 refused to return; 24 had left Albany; and nine more had died (Table 1).

A summary of the results of each examination was sent to the personal physician designated by the patient, who was instructed to consult his physician for interpretation of the findings and for execution of any indicated diagnostic or therapeutic procedures. Although nearly all participants designated a physician, only 60 per cent consulted them for a report.

Prevalence

At the first examination 70 individuals were found to have ischemic heart disease, a prevalence rate of 36 per 1,000. Thirty-seven men had survived a myo-

NOTE: Abbreviations Used in Tables

ASHD	Arteriosclerotic Heart Disease
AP	Angina Pectoris
AX	Abnormal Electrocardiographic Response to Exercise
EH	Essential Hypertension
IHD	Ischemic Heart Disease
MI	Myocardial Infarction
RHD	Rheumatic Heart Disease
Tbc	Tuberculosis

Table 2—Prevalence of Ischemic Heart Disease by Age (Cardiovascular Health Center—Examination I)

Age	Total	No Ischemic Heart Disease	Ischemic Heart Disease					
			Total Number	Rate per 1,000	MI		AP	AX
					Hist.	No Hist.		
Total	1,913	1,843	70	36	29	8	18	15
Under 40	84	83	1	12	1	–	–	–
40–44	665	658	7	11	3	–	2	2
45–49	675	647	28	41	10	4	8	6
50–54	481	447	34	71	15	4	8	7
55 and over	8	8	–	–	–	–	–	–

Table 3—Response to Self-Administered Questionnaire Item "Do You Feel Pain, Heaviness or Discomfort in the Chest?" (Cardiovascular Health Center—Examination I)

	Total	Response		Per cent Yes
		Yes	No	
Total	1,913	644	1,269	34
Normal	1,843	596	1,247	32
Ischemic heart disease	70	48	22	69

cardial infarction; 18 had angina pectoris; and 15 showed only an abnormal electrocardiographic response to exercise. The diagnosis of previous myocardial infarction could be established in almost all cases by the history alone (Table 2). The very high rate of false affirmative responses on the questionnaire to the question on chest pain indicated the necessity of skilled medical evaluation of this symptom (Table 3). Individuals considered to be clinically free of ischemic heart disease showed no consistent pattern in their responses to the question on chest pain in three consecutive questionnaires. About 24 per cent of the survivors of a myocardial infarction showed a normal resting electrocardiogram. Eighty-three per cent of those suffering from angina pectoris, without a previous, recognized myocardial infarction, likewise had a normal resting electrocardiogram. Twenty-three individuals with histories of ischemic heart disease were exercised and 19, or (again) 83 per cent, yielded normal electrocardiographic responses (Table 4). The problem of false-positive electrocardiographic responses to exercise is difficult to evaluate in the otherwise asymptomatic group of 15, but

Table 4—Electrocardiograms at Rest and Postexercise in Ischemic Heart Disease (Cardiovascular Health Center—Examination I)

	Electrocardiogram at Rest			
	MI		AP	
	Normal	Abnormal	Normal	Abnormal
Total	9 (24%)	28	15 (83%)	3
Normal postexercise	3	5	10	1
Abnormal postexercise	–	4	–	–
Not done	6	19	5	2

Table 5—Ballistocardiogram at Rest in Normal Individuals by Age and Relative Weight (Cardiovascular Health Center—Examination I)

Age	Less Than 20 Per cent Over Ideal Weight				20 Per cent or More Over Ideal Weight			
	Total	GR. II-III-IV	BCG Not Done	Per cent II-III-IV *	Total	GR. II-III-IV	BCG Not Done	Per cent II-III-IV *
Total	1,244	252	289	26.4	315	115	72	47.3
Under 40	56	–	50	–	13	–	9	–
40–44	465	69	102	19.2	117	32	24	34.4
45–49	434	101	86	29.3	112	47	24	52.8
50–54	284	81	51	35.2	71	34	15	60.7
55 and over	5	1	–	–	2	2	–	–

* By criteria of Brown and DeLalla [10] based on the total number of BCG's done.

it may be significant that one of these individuals has since sustained a myocardial infarction and two others have succumbed to the disease.

The ballistocardiogram proved to be of no diagnostic value. Approximately one-third of the subjects regarded as clinically free of ischemic heart disease showed abnormal ballistic patterns which correlated with increasing age and with overweight (Table 5). The postexercise ballistic patterns were of even less diagnostic value because of obscuring artefacts caused by tachycardia and tachypnea.

Incidence

In the 31 months from the initiation of the program to the completion of the second round of reexaminations, 18 deaths occurred, or an annual death rate of 3.6 per 1,000. These deaths are analyzed in Table 6. Forty new cases of ischemic heart disease were diagnosed in this period, an incidence rate of 9 per 1,000 per year. The 1,843 individuals considered clinically free of ischemic heart disease at the initial examination are considered to be the population at risk in calculating incidence rates of ischemic heart disease. The 231 nonrespondents are included in this denominator: 39 of them are lost from Civil Service records, while of the remaining 192 only one has died—of hepatic cirrhosis. The true incidence of ischemic heart disease is probably underestimated since nothing further is known of the health status of this nonrespondent group. On the other hand, the incidence rate for the whole 31 months could be increased from 22 per 1,000 to 23 per 1,000 by adding two deaths certified as arteriosclerotic heart disease and a third certified as coronary sclerosis (Table 6). Twenty-two of the new cases of ischemic heart disease had survived a first acute myocardial infarction while 10 others had developed angina pectoris. Eight, diagnosed as having ischemic heart disease because of the solitary manifestation of an abnormal electrocardiographic response to exercise, represent a category unique to this program (Table 7). The difference between the annual incidence rate of 9 per 1,000 observed in Albany, and the rate of 7 per 1,000 reported from the Los Angeles and the Framingham studies, can be accounted for by the inclusion of this unique group.[11, 12]

Table 6—Deaths During 31 Months' Observation (Cardiovascular Health Center)

Case	Age at Death	CVHC Dx	Date of Last Examination	Date of Death	Cert. Cause of Death
1	53	IHD–MI	3–53	4–53	ASHD
2	48	IHD–AX	9–53	1–54	ASHD
3	51	Diabetes mellitus IHD–MI	10–53	2–54	Diabetes mellitus
4	47	RHD	1–53	4–54	RHD
5	51	No disease	4–53	6–54	Coronary sclerosis
6	52	IHD–MI	5–53	8–54	ASHD
7	50	No disease	5–54	12–54	Carcinoma lung
8	48	No disease	10–53	3–55	Carcinoma bronchus
9	45	EH	7–54	3–55	Carcinoma kidney
10	56	Intermittent claudication	11–54	5–55	Rupture abdominal aorta
11	52	EH	1–55	8–55	ASHD
12	54	EH	11–54	12–55	Carcinoma pancreas
13	52	No disease	6–55	4–56	ASHD
14	56	IHD–AX	6–55	4–56	ASHD
15	54	HHD–Tbc.	3–55	6–56	Carcinoma lung
16	54	HHD	1–55	8–56	Failure of heart and blood circulation
17	54	IHD–MI	9–55	9–56	ASHD
18	51	IHD–MI	3–55	10–56	Rupture abdominal aorta

Etiologic Trends

The small number of cases of newly observed ischemic heart disease justifies only conjectures on characteristics which may predispose to or afford relative protection from ischemic heart disease. Neither job classification nor self-assessed ratings of "tension" could be related to the age-adjusted incidence rate of ischemic heart disease. Information concerning diet and habitual physical activity was insufficient to permit any deductions. Ischemic heart disease occurred more frequently as the

Table 7—Incidence of Ischemic Heart Disease During 31 Months' Observation (Cardiovascular Health Center)

Age	Population at Risk	New Cases		Manifestation		
		Number	Rate per 1,000	MI	AP	AX
Total	1,843	40	22	22	10	8
Under 40	84	—	—	—	—	—
40–44	665	10	15	6	2	2
45–49	675	14	21	7	3	4
50–54	481	16	33	9	5	2
55 and over	8	—	—	—	—	—

Table 8—Incidence of Ischemic Heart Disease During 31 Months' Observation by Serum Total Cholesterol Level mg/100 ml

(Cardiovascular Health Center)

Serum Total Cholesterol (mg/100 ml)	Population at Risk	New Cases	Rate per 1,000
Total	1,843	40	22
Less than 200	457	5	11
200–274	995	14	14
275 and over	209	13	62
Not done	182	8	44

No adjustment for age was made since cholesterol levels showed no tendency to increase with age over the span 39–55.

serum total cholesterol level rose. Thus, above a level of 275 mg/100 ml the risk of ischemic heart disease was six times greater than at a level of 200 mg/100 ml or less (Table 8). A detailed study of the lipoprotein patterns of this population showed that the discriminatory value of the individual cholesterol level was of a low order because of the large overlap in values of the clinically normal and abnormal groups.[13] A body weight up to 39 per cent over the Metropolitan Life Insurance Company standard weight carried little increased risk of ischemic heart disease,[14] while gross overweight, defined as a level 40 per cent or more over ideal weight, quadrupled the risk (Table 9). On the other hand, increase of body weight of more than 20 per cent above any weight level existing at the age of 25 doubled the risk of developing ischemic heart disease (Table 10). A soft, apical systolic murmur (Table 11), proteinuria or red

Table 9—Incidence of Ischemic Heart Disease During 31 Months' Observation by Relative Weight

(Cardiovascular Health Center)

Relative Weight	Population at Risk	New Cases	Rate per 1,000
Total	1,843	40	22
Less than 20% over ideal	1,419	27	19
20%–39% over ideal	335	8	24
40% or more over ideal	77	5	65
Not stated	2	—	—

Table 10—Incidence of Ischemic Heart Disease During 31 Months' Observation by Weight Gain from Age 25

(Cardiovascular Health Center)

Weight Gain from Age 25	Population at Risk	New Cases	Rate per 1,000
Total	1,843	40	22
Less than 20% gain	1,334	24	18
20% or more gain	415	14	34
Not stated	95	2	21

Table 11—Incidence of Ischemic Heart Disease During 31 Months' Observation by Presence or Absence of a Murmur

(Cardiovascular Health Center)

Murmur	Population at Risk	New Cases	Rate per 1,000
Total	1,843	40	22
Absent	1,707	35	21
Present-non-significant	108	5	46
Present-significant	24	—	—
Not stated	4	—	—

Table 12—Incidence of Ischemic Heart Disease During 31 Months' Observation by Urinalysis

(Cardiovascular Health Center)

Urinalysis	Population at Risk	New Cases	Rate per 1,000
Total	1,843	40	22
Albumin present	51	2	39
Albumin absent	1,777	38	21
Not stated	15	—	—
White blood cells in sediment	128	5	39
Red blood cells in sediment	55	2	36
Casts in sediment	26	2	—
Sediment absent	1,653	32	19
Not stated	15	—	—

or white blood cells in the urinary sediment (Table 12) were associated with double the risk of ischemic heart disease. Nonspecific abnormalities of the T wave in the resting electrocardiogram were associated with a three times higher incidence of ischemic heart disease

Table 13—Incidence of Ischemic Heart Disease During 31 Months' Observation by Resting Electrocardiogram

(Cardiovascular Health Center)

Resting Electrocardiogram	Population at Risk	New Cases	Rate per 1,000
Total	1,819*	40	22
Normal	1,689	32	19
Abnormal*	125	7	56
Not done	5	—	—

* Exclusive of 24 cases of rheumatic heart disease 18 of which were characterized by abnormal resting electrocardiograms.

(Table 13), an observation also recently made by others.[15] A family history of vascular disease, the somatotype, the density and distribution of hair on the head and body, the consumption of tobacco and of alcohol, and the level of the arterial diastolic blood pressure all failed to show significant associations with ischemic heart disease.

Summary and Conclusions

A group of 1,913 male office workers aged 39–55 years has been carefully studied over a three and a half year period. Seventy cases of ischemic heart disease were found on the initial survey, a prevalence rate of 36 per 1,000 population. Forty new cases of ischemic heart disease were found during the next two examinations, an annual incidence rate of 9 per 1,000 population. A carefully evaluated medical history is still the single best method of diagnosis. The electrocardiogram provides valuable confirmatory evidence of ischemic heart disease; nonspecific abnormalities of the T wave appear to be of prognostic importance; a significant number of diagnostic electrocardiographic abnormalities can be induced by exercise. Individuals with high levels of serum total cholesterol tend more often than normocholesterolemic individuals to develop ischemic heart disease.

This study shows the potentialities as well as the limitations of an intensive application of the best available clinical methods of diagnosing ischemic heart disease in a susceptible population. Until atherosclerosis can be recognized prior to the advent of its ischemic complications, the effectiveness of control measures cannot be evaluated. Meanwhile, prospective studies should amplify our present knowledge of the natural history of ischemic heart disease. Semicaptive populations, such as those of the Cardiovascular Health Center, provide a unique source of normative data as

well as an opportunity to pursue short-term research studies.

REFERENCES

1. Hilleboe, H. E.; James, G.; and Doyle, J. T. Cardiovascular Health Center. I. Project Design for Public Health Research. A.J.P.H. 44:851, 1954.
2. James, G.; Hilleboe, H. E.; Filippone, J. F.; and Doyle, J. T. Cardiovascular Health Center. II. First Year's Operation. A. General Observations and Hypertension. New York State J. Med. 55:774, 1955.
3. Abell, L. L.; Levy, B. B.; Brodie, B. B.; and Kendall, F. E. A Simplified Method for the Estimation of Total Cholesterol in Serum and Demonstration of Its Specificity. J. Biol. Chem. 195:357, 1952.
4. Keys, A., and Brozek, J. Body Fat in Adult Man. Physiol. Rev. 33:245, 1953.
5. Starr, I. On the Later Development of Heart Disease in Apparently Healthy Persons with Abnormal Ballistocardiograms. Am. J. M. Sc. 214:233, 1947.
6. Master, A. M. The Two-Step Exercise Electrocardiogram: A Test for Coronary Insufficiency. Ann. Int. Med. 32:842, 1950.
7. Erickson, L.; Simonson, E.; Taylor, H. L.; Alexander, H.; and Keys, A. Energy Cost of Horizontal and Grade Walking on the Motor-Driven Treadmill. Am. J. Physiol. 145:391, 1946.
8. Mattingly, T. W.; Fancher, P. S.; Bauer, F. L.; and Robb, G. P. The Value of the Double Standard Two-Step Exercise Tolerance Test in Detecting Coronary Disease: A Follow-Up Study of 1,000 Military Personnel. Army Med. Service Grad. Sch., Walter Reed Army Med. Center, Washington, September, 1954.
9. Nomenclature and Criteria for Diagnosis of Diseases of the Heart and Blood Vessels (5th ed.). New York: New York Heart Association, 1953.
10. Brown, H. R., Jr.; DeLalla, V., Jr.; Epstein, M. A.; and Hoffman, M. J. Clinical Ballistocardiography. New York: Macmillan, 1952.
11. Chapman, J. M.; Goerke, L. S.; Dixon, W.; Loveland, D. B.; and Phillips E. Measuring the Risk of Coronary Heart Disease in Adult Population Groups: The Clinical Status of a Population Group in Los Angeles Under Observation for Two to Three Years. A.J.P.H. Part 2, 47:4 (Apr.), 1957.
12. Dawber, T. R.; Moore, F. E.; and Mann, G. V. Coronary Heart Disease in the Framingham Study. Ibid., 1957.
13. Doyle, J. T.; DeLalla, L. S.; Baker, W. H.; Heslin, A. S.; and Brown, R. K. Serum Lipoproteins in Preclinical and in Manifest Ischemic Heart Disease. J. Chronic Dis. (In press.)
14. Metropolitan Life Insurance Company. Ideal Weights for Men. Statist. Bull. Metrop. Life Insur. Co. 23:6, 1942.
15. Keissling, C. E.; Schaaf, R. S.; and Lyle, A. M. Mortality Studies of Isolated Electrocardiograhic T-Wave Changes. 64th Ann. Meet. Assoc. Life Insurance Medical Directors, October, 1955.

IV. The Clinical Status of a Population Group in Los Angeles Under Observation for Two to Three Years

JOHN M. CHAPMAN, M.D., M.P.H., F.A.P.H.A.;
L. S. GOERKE, M.D., M.S.P.H., F.A.P.H.A.; WILFRID DIXON, Ph.D.;
DONALD B. LOVELAND; and EDWARD PHILLIPS, M.D.

A study of diseases of the heart in a working population was initiated in Los Angeles in 1949, assisted by the National Heart Institute, the California State Department of Public Health, and the Los Angeles City Health Department. A sample comprised of 2,252 persons out of 20,199 city civil service employees was examined to appraise practical technics sensitive to the early detection of diseases of the heart. In addition, the observations provide an opportunity to observe the occurrence of heart disease in a group of persons under periodic detailed clinical observation. This report summarizes the coronary disease experience, including prevalence, incidence, and mortality. The preliminary findings with reference to age, sex, physical demands, blood pressure, and height-weight characteristics are also presented.

The sample of employees chosen for study, stratified by age and sex, was selected randomly. In this sample 25 per cent refused the invitation to participate, or were not available. Each was replaced by an alternate of the same age and sex. There were 1,859 males and 393 females examined, including 1,899 classified white and 353 classified nonwhite. The persons ranged in age from 18 to 70 years. The median age at entry was 43.7 years. There are included 399 different civil service job classifications, varying in number and type from one astronomer, one councilman, one cook-housekeeper, and two blacksmiths to 176 maintenance laborers. The subjects received three examinations at intervals of 12 to 18 months. The interval from the first to the third examination ranged from 28 to 32 months in 90 per cent of the persons in the study. The composition of the study population by age, sex and race is presented in Table 1.

The examinations were performed by internists specializing in cardiology. The same physicians participated throughout the study. However, all diagnoses were recorded by one of these cardiologists. Diagnostic procedures were based upon the New York Heart Association criteria.[1] Technics employed included questionnaire history, physical examination, electrocardiogram (12 or 13 leads), fluoroscopy of the chest, electrokymogram, chest x-ray, vital capacity determination, urine analysis, blood count, sedimentation rate, hematocrit, blood sugar, and serum cholesterol. The results of the initial clinical examinations are previously published.[2] The subsequent clinical status of the study population, together with the results of certain diagnostic technics, are recently reported.[3] A lipoprotein study, which includes specimens from this group, is to be published by other authors.[4]

The authors are associated with the Department of Preventive Medicine and Public Health, Schools of Medicine and Public Health, University of California at Los Angeles.

This study was supported in part by a contract with the National Heart Institute, Public Health Service; in part by the California State Department of Public Health.

Table 1—Composition of Study Population According to Age, Sex, and Race

Age at Entry	All Persons	Male				Female			
		Total	White	Negro	Oriental	Total	White	Negro	Oriental
Under 20	4	–	–	–	–	4	3	1	–
20–29	368	273	198	74	1	95	71	17	7
30–39	554	461	359	99	3	93	82	10	1
40–49	554	447	382	64	1	107	102	5	–
50–59	538	462	413	49	–	76	74	2	–
60–69	231	213	197	16	–	18	17	1	–
70	3	3	3	–	–	–	–	–	–
Total	2,252	1,859	1,552	302	5	393	349	36	8

Prevalence

Table 2 summarizes the prevalence of diseases of the heart based upon examination and diagnosis of the individuals as they entered the study. Observe that 7.3 per cent were diagnosed as having diseases of the heart, including hypertensive heart disease (3 per cent), coronary and hypertensive heart disease (1.2 per cent), and coronary disease without hypertensive heart disease (1.3 per cent). Since only 18 of the 165 cases were females, some of the tables omit data for females.

Table 2—Prevalence of Diseases of Heart in Study Population

Index Examination Diagnoses	Number of Persons	Per cent of Population Examined
Normal heart	2,007	89.1
Possible or potential heart disease	80	3.6
Diseases of the heart (total)	165	7.3
Hypertensive heart disease	67	3.0
Coronary and hypertensive	26	1.2
Coronary	29	1.3
Rheumatic	19	0.8
Rheumatic and hypertensive	4	0.2
Other etiologic type	7	0.3
Etiology unknown	13	0.6
Total	2,252	100

Table 3 shows the prevalence of diseases of the heart in males according to age. Hypertensive heart disease was the most prevalent, ranging from 0.5 per cent of males under 40 to 11.8 per cent of males 55 to 70 years of age. The association of coronary artery disease and hypertensive heart disease is reflected in the proportion of persons having both diseases. The proportion is much greater than could be expected if both diseases occurred independently (Table 3).

Coronary disease was diagnosed in 50 males (2.7 per cent) and in 5 females (1.3 per cent). Relatively few cases were discovered under 40 years of age. Less than 2 per cent of the males aged 40 to 54 years and approximately 9 per cent aged 55 to 70 years were diagnosed coronary disease. These include persons with prior diagnosis and previous knowledge of coronary disease as well as newly discovered cases apparently diagnosed for the first time on entry to this study. For example, 14 of the 50 males diagnosed coronary disease gave

Table 3—Prevalence of Diagnosed Diseases of the Heart in Males on Entry to Study

Age in Years at Entry	Number of Males	Coronary Disease		Coronary and Hypertensive Heart Disease		Hypertensive * Heart Disease		Other Heart Disease		Total with Heart Disease	
		No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
Under 40	734	1	0.1	1	0.1	3	0.4	16	2.2	21	2.9
40-54	692	6	0.9	4	0.6	23	3.3	12	1.7	45	6.5
55-70	433	20	4.6	18	4.2	31	7.2	12	2.8	81	18.7
All ages	1,859	27	1.5	23	1.2	57	3.1	40	2.2	147	7.9

* Excludes 4 persons with rheumatic and hypertensive heart disease.

a history of prior "coronary thrombosis," and six gave a history of previous "heart attack." Based upon the questionnaire history, therefore, 30 of the 50 males were newly diagnosed cases.

Mortality

Of the 55 persons (men and women) with coronary disease on entry to the study, six were dead by the time of the third examination, 24 to 36 months later, nine withdrew from observation, 33 were still diagnosed as coronary disease, one as hypertensive heart disease, four as possible or potential heart disease, and two as normal heart. A search for deaths among the entire study population included matching of names and other identifying information against all deaths registered in California through December 31, 1954. As this search was made in the spring of 1956, it is likely that the registered deaths through 1954 are reasonably complete. Table 4 describes total mortality according to clinical status at entry (both sexes and all ages). As the dates of entry to the study ranged over a period of 19 months, from December, 1949, to July, 1951, the "exposure" time to December, 1954, varied among the participants. Therefore, age-specific mortality rates are based upon exactly 41 months' experience for each individual subsequent to his own entrance (first) examination (Table 5). Sixty-two deaths occurred within 41 months, all but three in males. Of the deaths classed as arteriosclerotic heart disease, including coronary disease, all but two of the certificates of death mentioned coronary occlusion,

Table 4—Total Deaths According to Clinical Status at Entry

Clinical Status at Entry	Number of Persons	ASHD incl. Coronary Disease		Other CVD		Non CVD		All Deaths to December 31, 1954	
		No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
Normal heart	2,087	14	0.7	4	0.2	22	1.1	44*	2.2
Coronary	29	4	13.8	0	0.0	2	6.9	6	20.7
Coronary and hypertensive	26	2	7.7	0	0.0	1	3.8	3	11.5
Hypertensive heart disease	67	2	3.0	5	7.0	1	1.5	8	11.5
Other heart disease	43	1	2.3	2	4.7	1	2.3	4	9.3
Possible or potential heart disease	80	3	3.7	0	0.0	1	1.3	4	5.1
Totals	2,252	26	1.2	11	0.5	28	1.2	69*	3.1

* Includes persons with certificate of death and cause of death not available.

Table 5—Mortality Within 41 Months of Entry to Study by Age and Sex

Age in Years at Entry	Number of Persons	Total Deaths		Total Cardiovascular Disease		Arteriosclerotic Heart Disease	
		No.	Per cent	No.	Per cent	No.	Per cent
Under 40							
Male	734	4	0.5	0	–	0	–
Female	192	1	0.5	0	–	0	–
Total	926	5	0.5	0	–	0	–
40–54							
Male	692	18	2.6	12	1.7	9	1.3
Female	150	2	1.3	0	–	0	–
Total	842	20	2.4	12	1.4	9	1.1
55–70							
Male	433	37	8.5	23	5.3	16	3.7
Female	51	0	–	0	–	0	–
Total	484	37	7.6	23	4.8	16	3.3
All ages							
Male	1,859	59	3.2	35	1.8	25	1.3
Female	393	3	0.8	0	–	0	–
Total	2,252	62	2.8	35	1.6	25	1.1

coronary thrombosis and/or myocardial infarct. The two remaining specified "arteriosclerotic heart disease" as the cause of death. The age factor predominates in the total death rate, total cardiovascular disease deaths, and in deaths from coronary disease. Nearly half (45 per cent) of the total deaths among males 40–70 years of age are ascribed to coronary disease. The 41-month coronary disease death rate is greater in males aged 55 to 70 years (3.7 per cent) than in males aged 40–54 years at entry (1.3 per cent). These rates adjusted to annual mortality rates are 1.1 and 0.4, respectively. Since the rates are expressed according to age at entry, they will obviously rise as the age of the study population increases.

Observation of comparative mortality from coronary disease according to the clinical status of males at entry to the study is limited by the small number of deaths which have occurred. Of 48 men 40 years of age and over who were diagnosed coronary disease at the first examination, nine (18.8 per cent) died within 41 months of this examination, including six (12.5 per cent) of coronary disease. Of 955 males 40 or more years of age with normal heart at entry, 31 (3.2 per cent) died, including 13 (1.4 per cent) of coronary disease. Since persons with normal heart are younger than persons with heart disease, it will be necessary to study narrower age groups when additional data are available.

Coronary disease deaths, within two age groups, among persons with normal heart and with coronary disease are summarized in Table 6. Within the limitations imposed by the small number of deaths, variations within the age groups, and the disparity in size of the diagnostic groups, there occurred among males entering the study with a diag-

Table 6—Total Deaths and Coronary Disease Deaths in Males by Age and Diagnosis at Entry

Age in Years at Entry	Cardiac Diagnosis at Entry	Number of Males		Deaths Within 41 Months						Annual Rate †		
				Total		Total CVD		ASHD incl. Coronary		Total	Total CVD	ASHD incl. Cor.
		No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	Per cent	Per cent	Per cent
40–54	Normal heart	626	100	10	1.6	5	0.8	5	0.8	0.5	0.2	0.2
	* Coronary disease	10	100	2	20.0	2	20.0	2	20.0	5.9	5.9	5.9
55–70	Normal	329	100	21	6.4	12	3.7	8	2.4	1.9	1.1	0.7
	* Coronary disease	38	100	7	18.4	4	10.5	4	10.5	5.4	3.1	3.1
Total over 40	Normal heart	955	100	31	3.2	17	1.8	13	1.4	0.9	0.5	0.4
	* Coronary disease	48	100	9	18.8	6	12.5	6	12.5	5.5	3.7	3.7

* Includes persons with coronary and hypertensive heart disease.
† Annual rate determined by multiplying 41-month rate by 12/41.

nosis of coronary disease, at age 40–54 years and at 55–70 years, higher death rates from coronary disease than in males with normal heart at entry. At ages 40–54, two of 10 who were diagnosed coronary disease died as compared to 10 of 626 diagnosed normal heart. Both of the deaths in the coronary disease group and five deaths in the "normal" heart group were ascribed to coronary disease. At ages 55–70 years, seven of 38 (18.4 per cent) who were diagnosed coronary disease died within 41 months, including four (10.5 per cent) deaths ascribed to coronary disease. Twenty-one of 329 (6.4 per cent) diagnosed normal heart died, including eight deaths caused by coronary disease (2.4 per cent). The status of males in these two age groups 41 months after the entrance examination is summarized as follows:

Age in Years	Clinical Diagnosis at Entry	Number of Males	Status 41 Months After Diagnosis: Living	Dead (All Causes)	Deaths Ascribed to Coronary Disease
40–54	Coronary disease	10	8	2	2
	Normal heart	626	616	10	5
55–70	Coronary disease	38	31	7	4
	Normal heart	329	308	21	8

It is important to note that among all 19 male employees who died of coronary disease, clinical coronary disease was detected in but six, and the remaining 13 had no clinical evidence of heart disease at entry to study.

Incidence

Observation of the occurrence of diagnosed cases and deaths among persons entering the study with a diagnosis of normal heart provides data on the incidence of coronary disease in this group. Of 1,653 males diagnosed normal heart on first examination, 39 (2.4 per cent) were discovered with coronary disease (including coronary and hypertensive heart disease) within 24 to 36 months. These include 26 diagnosed on or before the third examination, three diagnosed on the second examination who

Table 7—Occurrence of New Cases of Coronary Disease Within 30-Month Period Among Persons Diagnosed Normal Heart on Entry to Study, by Age and Sex

Age at Entry	Sex	Number of Persons		Withdrew		New Cases: Total		New Cases: Diagnosed on Examination		New Cases: Death Certificate	
		No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
Under 40	Male	698	100	99	14.2	2	0.3	2	0.3	–	0
	Female	178	100	32	18.0	–	0	–	0	–	0
40–54	Male	626	100	37	5.9	13	2.1	10	1.6	3	0.5
	Female	139	100	10	7.2	1	0.7	1	0.7	–	0
55–70	Male	329	100	46	14.0	24	7.3	17	5.2	7	2.1
	Female	37	100	6	16.2	2	5.4	2	5.4	–	0
All ages	Male	1,653	100	182	11.0	39	2.4	29	1.8	10	0.6
	Female	354	100	48	13.6	3	0.8	3	0.8	–	0

withdrew from observation, and 10 deaths ascribed to coronary disease prior to the third examination. The interval from the first to the third examination was approximately 30 months, or 2.5 years for the study population as a whole. The incidence was 2.1 per cent among males aged 40–54 years and 7.3 per cent among males aged 55–70 years (Table 7). Mortality from coronary disease in these two age groups was 0.5 per cent and 2.1 per cent, respectively. Of the new cases among males, three of the 13 aged 40–54 years (23 per cent), and seven of the 24 aged 55–70 years (29 per cent) were deaths.

The clinical status of the persons who withdrew from observation prior to the third examination has an important bearing on these coronary disease risk measurements. "Withdrawals" in this study are defined as persons who discontinued clinical observation prior to the third examination, did not return, and are not known to be dead. The incidence of clinical coronary disease in the withdrawal group is unknown. A follow-up study to determine the characteristics of persons who withdrew is under way to appraise the occurrence of heart disease in this group as compared to persons present at all three examinations. A higher coronary disease rate among the persons who withdrew would result in higher incidence than recorded here (Table 7). Coronary disease morbidity and mortality rates among males with normal heart on first examination, adjusted to annual rates,* are as follows:

Age at Entry	Number of Males Observed	Annual Incidence (Per cent)	Annual Mortality (Per cent)
Under 40	698	0.1	0.0
40–54	626	0.8	0.2
55–70	329	2.9	0.9

Occupation and Physical Exertion

Of the 399 civil service job classifications included in the study, 163 were represented by one employee, 188 by two to nine employees, 44 by 10–50 employees and each of four by more than 50 employees. While the physical demands of any one job classification

* Annual rate determined by multiplying 24–36 month rate by 12/30.

Table 8—New Cases of Coronary Disease * Among Males Aged 40 to 70 Years by Physical Exertion Class

Occupation According to Physical Exertion	Number Diagnosed Normal Heart First Examination	New Cases of Coronary Disease on or Prior to Third Examination		100 x Actual/Expected
		No. Diagnosed	No. Expected †	
Sedentary	114	3	4.2	71
Light	431	17	16.7	102
Medium	256	8	9.4	85
Heavy	137	8	5.8	138
Doubtful	17	1	0.7	143
All classes	955	37	37.0	100

* New cases include persons diagnosed coronary disease on third examination, deaths from arteriosclerotic heart disease before the third examination, and persons diagnosed coronary disease on the second examination among those not receiving the third examination.

† Expected cases obtained by applying age-specific rates for all classes to the age distribution of the specified physical exertion class.

may be somewhat similar for all employees of that class, variations in physical exertion are known to occur on and off the job. Appraisal of the total physical demands upon each person in the study was not carried out. The occupations represented in the study are grouped by degree of physical exertion according to a list adapted by the National Office of Vital Statistics from a United States Department of Labor coding system. Persons whose job titles did not permit a decision are grouped in the "doubtful" physical exertion class. Of the persons classed in "sedentary" work, 85 per cent were employed in clerical, accounting, library, and similar jobs. Approximately 50 per cent at "light" physical exertion were directors, plant operators, engineers, inspectors, or in similar occupations. In the "medium" exertion class, 75 per cent were employed as warehousemen, janitors, equipment operators, servicemen, and the like. Maintenance laborers, gardeners, and carpenters comprised 90 per cent of the "heavy" physical exertion class.

The number of newly diagnosed cases of coronary disease among males with normal heart on first examination, according to physical exertion class, is shown in Table 8. The age-specific rates for the total group were applied to the populations in each physical exertion class to determine the expected number of cases in each class. There is close agreement between the number of cases diagnosed and the number expected. Within this group of employees, the physical demands of the jobs do not appear to have had a significant influence on the occurrence of coronary disease during the period of observation. It must be borne in mind that these individuals were in these jobs for some time previous to the study and were diagnosed normal heart on their entrance examination.

The effects of duration of employment in the physical exertion class and of economic status are under investigation.

Weight

In our preliminary studies to determine the relationship of obesity to coronary disease, a height-weight index is used to classify males.[5] This index has

Table 9—Incidence (Per cent) of Coronary Disease Between First and Third Examinations Among Males According to Height-Weight Index, by Age

Age at Entry	All Values	Height-Weight Index: Less than 12.0 (Heavy)	12.0–12.4 (Med. Heavy)	12.5–12.9 (Med. Light)	13.0 and Over (Light)
40–54					
Number at risk	626*	134	190	191	110
New cases	13	7	2	3	1
Incidence (per cent)	2.1	5.2	1.1	1.6	0.9
55–70					
Number at risk	329	77	103	92	57
New cases	24	4	8	10	2
Incidence (per cent)	7.3	5.2	7.8	10.9	3.5
40–70					
Number at risk	955*	211	293	283	167
New cases	37	11	10	13	3
Incidence (per cent)	3.9	5.2	3.4	4.6	1.8

* Includes one person for whom height and index are unknown.

been used in anthropologic studies of the population. Although it may not correspond in all cases to a clinical diagnosis of obesity, it does permit measurement of the risk of coronary disease in the group studied according to one index of weight relative to height.

Based upon measurement of height to the nearest inch, divided by the cube root of the weight, males diagnosed normal heart on entry are grouped into four classes ranging from heavy to light. New cases of coronary disease, including deaths, occurring between the first and third examinations are shown in Table 9. Among males 40–54 years of age, the incidence is highest in the heavy class (5.2 per cent) and lowest in the light class (0.9 per cent). Seven new cases occurred among 134 men diagnosed normal heart on entry and classed as heavy compared to one new case among 110 men in this age group classed as light. In the 55–70-year-age group, the incidence of coronary disease among males in the light height-weight index classes is similar to the incidence among males in the heavy classes (Table 9). Within each of these broad age groups, the differences in incidence are not accounted for by age differences among the height-weight classes. The differences at 40–54 years are statistically significant at the 5 per cent level.

Blood Pressure

Tables 10 and 11 are presented to illustrate preliminary data on the incidence of coronary disease in males according to blood pressure.

The population at risk includes all males except those diagnosed coronary disease on entry to the study. New cases include persons diagnosed coronary disease on or before the third examination and coronary disease deaths prior to the third examination.

The incidence of coronary disease among males aged 40–54 years with a diastolic blood pressure of 95 mm Hg or over was higher than in males in the

Table 10—Incidence of Coronary Disease in Males According to Diastolic Blood Pressure and Age

Age at Entry	Diastolic Pressure	No. of Males	New Cases	Per cent
40–54				
	Less than 75	109	2	1.8
	75–84	270	4	1.5
	85–94	204	4	2.0
	95 and over	99	7	7.1
	Total	682	17	2.5
55–70				
	Less than 75	50	4	8.0
	75–84	156	17	10.9
	85–94	113	7	6.2
	95 and over	76	5	6.6
	Total	395	33	8.4

same age group with lower diastolic blood pressure on entry to the study (Table 10). The incidence was also higher among males aged 40–54 years with systolic blood pressure of 145 mm Hg or over than in persons in this age group who had a lower systolic blood pressure at the entrance examination (Table 11). The differences observed in incidence of coronary disease according to diastolic and systolic blood pressure in males 40–54 years of age are statistically significant at the 5 per cent level. Significant differences in incidence according to entrance examination diastolic or systolic blood pressure are not observed among the males aged 55–70 years.

Table 11—Incidence of Coronary Disease in Males According to Systolic Blood Pressure and Age

Age at Entry	Systolic Pressure	No. of Males	New Cases	Per cent
40–54				
	Less than 115	209	4	1.9
	115–124	182	1	0.5
	125–134	144	4	2.8
	135–144	73	2	2.7
	145 and over	74	6	8.1
	Total	682	17	2.5
55–70				
	Less than 125	146	12	8.2
	125–144	150	13	8.7
	145–164	57	5	8.8
	165 and over	42	3	7.1
	Total	395	33	8.4

Summary

A sample of Los Angeles City Civil Service employees, chiefly males, was observed clinically for two to three years for the occurrence of diseases of the heart. Based upon diagnosis at the entrance examination, the prevalence of coronary disease in males, including combined coronary and hypertensive heart disease, was 2.7 per cent. Prevalence ranged from 0.2 per cent of males under 40 years of age to 8.8 per cent at 55–70 years of age.

The annual death rate from arteriosclerotic heart disease including coronary disease was 0.4 per cent among male employees with clinically normal heart on entry and 3.7 per cent in men diagnosed coronary disease. Only six of the 19 males who died of coronary disease within 41 months were diagnosed coronary disease on entry to the study.

The average annual incidence of coronary disease in males with normal heart on entry was 0.1 per cent under 40 years of age, 0.8 per cent at 40–54 years, and 2.9 per cent at 55–70 years of age.

Preliminary findings are presented on the occurrence of coronary disease according to physical exertion, weight, and blood pressure.

ACKNOWLEDGMENT—Use of tabulating equipment for the present study was provided in part by the Office of Naval Research and the Office of Ordnance Research, United States Army.

REFERENCES

1. Nomenclature and Criteria for Diagnosis of Diseases of the Heart (4th ed.). New York: New York Heart Association, 1947.
2. Phillips, E.; Chapman, J. M.; and Goerke, L. S. Relative Values of Techniques Used in Detection of Heart Disease. Am. Heart J. 45:319 (Mar.), 1953.
3. Chapman, J. M.; Goerke, L. S.; Dixon, W.; Phillips, E.; and Loveland, D. B. A Study of Diseases of the Heart in a Working Population. Report to the California State Department of Public Health. (Unpublished.)
4. Report of the Committee on Lipoproteins and Atherosclerosis. (To be published.)
5. Sheldon, W. H. Atlas of Men: A Guide for Somatotyping the Adult Male of All Ages. New York: Harpers, 1954.

V. An Epidemiological Investigation of Coronary Heart Disease in the California Health Survey Population

ROBERT M. DRAKE, M.D., M.P.H.; ROBERT W. BUECHLEY; and LESTER BRESLOW, M.D., M.P.H., F.A.P.H.A.

The epidemiological method is being used increasingly for the investigation of coronary heart disease. The frequency and distribution of coronary heart disease in populations provide clues for further investigation and establish a framework against which other research findings can be assessed. Furthermore, epidemiology provides a method for examining etiological hypotheses in population groups rather than in the laboratory or clinic.

Until recent years epidemiological knowledge about this disease came mainly from death certificates, necropsy examinations, and clinical records. All too often the cases came from undefined populations, for which descriptive data were uncertain or lacking. Moreover, the representativeness of the cases themselves was open to question. It was usually difficult even to estimate what proportion of the total incidence or prevalence in the population was represented by the cases under investigation.

The reports presented here provide examples of the application of epidemiological methods to coronary heart disease. Two studies [4, 6] deal with samples of civil service employee populations, and a third is concerned with a community population sample.[3] Our paper reports an inquiry into coronary heart disease in California—based on a source of information not previously used for this purpose—a general population morbidity survey. The use of a sample survey for epidemiological purposes gives confidence in generalization to the whole population. The total study population comprised persons selected for interview by the California Health Survey. The latter, a household survey sample representative of the civilian population of California, provided a defined population about whom considerable social and demographic data were collected. In this survey population 250 persons were reported to have had arteriosclerotic heart disease, coronary heart disease, or angina pectoris.[2] *

Some disadvantages in this approach to selection of cases must be noted. One could not expect that all the cases of coronary heart disease in such a population would be reported. Nor were the reported cases necessarily representative of all coronary heart disease cases in the study population. However, it seemed possible either to minimize or at least to describe these limitations by defining and studying other classes of cases in the survey population.

Since the initial case material resulted from respondent's reports, some inaccuracy of diagnostic statements appeared likely. However, all reported cases were said to have been medically attended, so that obtaining a physician's report was a possibility.

---

* These three classes are coded 420.0, 420.1, and 420.2 by the International Statistical Classification. To avoid awkward usages, the term "coronary heart disease" will include all three subclasses. To indicate a specific subclass, the ISC code number will be used.

The authors are associated with the State Department of Public Health, Berkeley, Calif.

This study was supported in part by a contract with the Heart Disease Control Program, Public Health Service; in part by a research grant from the National Institutes of Health.

The difficulty of obtaining accurate information about events occurring in the past requires no amplification here.

Several advantages in this situation may also be mentioned. The survey population provided a representative group of persons without reported coronary heart disease for purposes of comparison with the cases. It appeared relatively inexpensive to collect additional data for cases and noncases. The availability of a case-control series permits examination of several etiological hypotheses at the same time by the collection of appropriate data.

A study of these coronary heart cases was undertaken in November, 1955, with three objectives:

First, to obtain medical verification for the statement of diagnosis as reported by the respondent to the California Health Survey interviewer.

Second, to obtain additional data about hypothesized etiological factors. Tests of the many current hypotheses by different methods in different settings may help to clarify their relative importance.

Third, to describe the social impact of coronary heart disease.

The work done in the first year—the study plan, the kinds and amounts of data collected—is reported here. Examples of the types of data being obtained are also included.

Methods and Materials

A. Selection of Cases

The California Health Survey was a household sample survey designed to measure illness in the general population of the state. Detailed information on all types of illness and injuries was sought. Among the questions asked when a condition was reported were, "When did it start?", "Was a doctor seen about it?", and "What did the doctor say it was?". Relevant demographic information was also collected. The plan of study has been summarized elsewhere [2] and a monograph describing the findings is in preparation.

Representative of the population of California the survey covered about 30,000 persons in 10,000 households, from May, 1954, through April, 1955. The sample was weighted. This was especially true for rural and new construction areas. The actual number of individual persons reported in the California Health Survey as having coronary heart disease was 224. When the sample was adjusted for weights the weighted number of persons with coronary heart disease, representative of the California population, is 250. This weighted number is used throughout this report.

B. Possible Categories of Cases

The coronary heart disease cases which might occur in the California Health Survey population could be divided into the following categories:

1. Persons who were reported in the survey to have coronary heart disease. Coded to ISC codes 420.0, 420.1, and 420.2 by the survey, these 250 persons comprise the cases studied thus far.
2. Persons (over 30 years of age) who were reported to have "heart disease," unspecified. Coded to ISC code 434.3 by the survey, these 296 persons are currently under study. Incomplete results indicate that about one-third of these persons will be verified as having coronary heart disease.
3. Persons for whom neither coronary heart disease nor heart disease, unspecified, was reported at interview, but who died of the disease within 12 months after interview. A study of these persons is being planned.
4. Persons with diagnosed coronary heart disease who, themselves, or whoever responded for the household, did not report anything codable to coronary heart disease or "heart disease," unspecified, although they may have reported some other condition.
5. Persons with diagnosable coronary heart disease who have not been so diagnosed. These would correspond to the "newly diagnosed" in a case-finding survey.

The California Health Survey itself could disclose only categories 1 and 2.

Table 1a—Weighted Number of Persons Reported to Have Coronary Heart Disease (ISC 420.0, 420.1, and 420.2) in California Health Survey by Age and Sex

Sex	Total	Age Groups									
		35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75–84	85 and Over
Total	250	5	12	11	20	38	50	42	32	34	6
Male	150	4	10	9	17	23	30	19	19	16	3
Female	100	1	2	2	3	15	20	23	13	18	3

Category 3 could be determined by checking the survey population against death registration records. It was not feasible to examine the survey population medically so that categories 4 and 5 are beyond reach of this inquiry.

C. Description of Coronary Heart Disease Cases; Category 5 so Reported; and Category 2, Reported as Heart Disease, Type Unspecified

The listing of persons coded "arteriosclerotic heart disease including coronary disease" (codes 420.0, 420.1, and 420.2) yielded 250 persons.

The listing of persons coded "heart disease" (code 434.3) yielded 296 persons 30 years of age and over. Those under this age were eliminated as being unlikely to have coronary heart disease. About one-third of the 296 persons have now been interviewed, with indications that about one-third have coronary heart disease. Extension of this finding to the remainder gives an estimate of 80–100 coronary cases. Characteristics of the first two categories, as found to date, appear in Tables 1 and 2.

D. Estimating the Number of Deaths from Coronary Heart Disease, Category 3

Since the survey population is representative of the total population, all rates applicable to the latter can be applied to the survey population. Application of California 1954 death rates to the survey population gives an expected 60–100 coronary heart disease deaths in one year. Coronary heart disease deaths actually observed among those reported as having the disease at the time of the survey (category 1) numbered 10 within one year after interview of whom five

Table 1b—Weighted Per cent of Persons Reported to Have Coronary Heart Disease (ISC 420.0, 420.1, and 420.2) in California Health Survey by Age and Sex

Sex	Total	Age Groups									
		35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75–84	85 and Over
	Per cent										
Total	100	2	5	4	8	15	20	17	13	14	2
Male	100	3	7	6	11	15	20	13	13	10	2
Female	100	1	2	2	3	15	20	23	13	18	3

Table 2—Age, Sex, and Race Characteristics of Coronary Heart Disease Cases and Heart Disease Unspecified Cases in the California Health Survey Population

	Coronary Heart Disease Cases (11/1/1956)				Unspecified Heart Disease Over 30 Years of Age	California Health Survey Population Over 25 Years of Age
		Physician's Reports				
	Total	Verified Coronary	Verified Not Coronary	Not Verified and No Response	Total	
	250=100%	140=100%	35=100%	75=100%	296=100%	100%
Age						
44 and under	7%	2%	11%	13%	15%	51%
45–54	12	16	3	9	14	20
55–64	35	37	43	32	24	15
65–74	30	31	20	31	28	14
75 and over	16	14	23	15	19	
Sex						
Male	60	69	29	57	49	48
Female	40	31	71	43	51	52
Race						
White *	100	100	100	100	94	91
Negro	—	—	—	—	3	3
Other †	—	—	—	—	3	6

* Excludes persons of Spanish surnames.
† Includes persons of Spanish surnames.

were males under 65 years of age. Fifty to 90 deaths not to persons in category 1 must, then, have occurred to persons in groups 2, 3, 4, or 5.

E. Estimating Unreported and Undiagnosed Coronary Heart Disease Cases, Categories 4 and 5

There are limitations to using prevalence data from studies of selected populations to provide estimates of prevalence in the general population. Nonetheless, keeping these reservations in mind, estimates may be made of the total prevalence to be expected in the California Health Survey population. Prevalence data have been obtained in more intensive case-finding surveys based upon screening and diagnostic examinations. Thus, as examples, Table 3 shows prevalence rates for males, aged 35–64, from selected California studies.[6, 7]

Applying these rates to the California Health Survey population of males aged 35–64 gives estimates of 173 and 171 total coronary heart cases, respectively. The 93 males aged 35–64 actually reported in category 1 from the California Health Survey thus appear to be about 50 per cent of the estimated total cases. Category 2 would add about 20 per cent to this. Thus about one-third of the expected cases of coronary heart disease in this age-sex group were not and could not be recognized by the methods used in the California Health Survey.

F. Selection and Matching of Control Groups

In order to test several etiological hypotheses it was desired to compare cer-

Table 3—Coronary Heart Disease Prevalence Rates by Age Group Per 1,000 Males Selected California Studies

	Number of Persons	All Ages (Crude Rate)	Age Groups				
			20–29*	30–39	40–49	50–59	60–61
Phillips, et al. [4]	1,859	26.4	0	4.3	11.2	47.6	92.6
Longshoremen †	3,694	27.9	—	3.9	13.5	41.9	97.4
California Health Survey †	7,951	11.7	0	1.6	8.9	24.2	45.8

* California Health Survey, ages 25–29.
† Unpublished data, California Department of Public Health.

tain characteristics for persons reported as having coronary heart disease with those of persons representative of the survey population, but not reported as having any cardiovascular condition. Such comparisons were also needed to attain the third objective of the study—determining the social impact of the disease. Since occurrence of coronary heart disease is closely related to age and sex, randomly selected controls of matching age and sex were selected from the California Health Survey population. Matching on several other available items—for example, race or ethnic group, income level, occupation, education, and marital status—was considered. In our opinion, none of these characteristics have such a well established relationship to coronary heart disease as to warrant controlling at this time in this population group.

G. Development of Questionnaires

A four-page questionnaire was developed to meet the three objectives. The first two pages obtained additional data about etiological factors, the third page explored the social impact of the disease, and on the fourth page was an authorization to the patient's physician to give additional information to the department. The questionnaire used in this inquiry is appended to allow inspection of the specific items (pages 54–57).

The many etiological hypotheses incorporated in the questionnaire were drawn from a variety of sources, most of which are described and referenced in Miller, et al.[5] Birthplace questions, gathered as part of the identifying information, allow a distribution into nationality groups. Height and weight, at stated ages, make possible tabulations of body build, further refinable by respondent's statements of muscularity and fatness. A measure of physiological aging was attempted by asking the age at which reading glasses or bifocals were first needed.[1] The respondents were also asked to place themselves on a temperament scale with respect to the average. An inquiry was made on occupation and industry, including physical activity of the job, nervous strain of the job, hours spent standing, and years worked. Then recreational activity was requested, paying particular attention to athletic achievement in high school and college. Maintenance of regular recreational activities in adult life was inquired about. A detailed dietary check list of fat-containing foods was to be filled in and salt intake pattern was asked. The fact of being on a diet, and whether or not this was on doctor's orders, was requested. A check on family longevity was made by asking parent's age at death and cause of death, or attained age, if living. A final etiological question was asked on cigarette

smoking history, both amount and duration.

Social impact of the disease was explored through questions on changes in incomes, resources, employment, housing, social life, and social status.

The authorization to physicians was the prime purpose of the last page but, to lead up to this, questions about various chronic diseases were asked.

Medical verification by a physician's report was sought only for the cases. Since the physicians named by the respondents were located throughout the state, a letter-questionnaire to physicians was developed to obtain the desired information. The physicians were advised that the inquiry was about cardiovascular disease, but the questionnaire did not state that coronary heart disease was specifically under study.

H. Data Collection

The primary approach to the respondents was through the mailing of questionnaires to the addresses given at the time of the California Health Survey. Two weeks after the first mailing a second mailing went to those who had not responded. Two weeks later a third mailing was sent to half of those persons not yet heard from. The remainder of the responses were obtained through personal interviews.

As completed questionnaires were received, a photostat was made of the authorization section of the questionnaire. This, together with the letter-questionnaire, was mailed to the physician named by the patient. When no reply was received within one month, a second letter went to the physician. No personal follow-up of physician nonrespondents has yet been made, due to a satisfactory rate of good returns from mailing and to lack of available time.

The study was presented to the respondents as being a special health inquiry into chronic diseases. Coronary heart disease was not specifically mentioned, although some persons with this condition probably assumed that this was the condition under study. With this indirect approach it was not practicable to closely date events occurring at or before the date of onset or diagnosis of coronary heart disease. Various devices were used to obtain information dealing with events of the past; some were obtained as lifetime history, some as of a specific age, and some as of the year 1950.

Of the total 512 questionnaires mailed, 217 considered satisfactory were received by mail, some from outside the state. This was 47 per cent of the total. Interviewing brought in an additional 210 satisfactory responses. There were 61 refusals and 24 could not be located by the interviewer or had left the state. The response rate was best in the nonmetropolitan areas of the state and poorest in the San Francisco Bay Area. In all, satisfactory responses were obtained from 427 persons or 83 per cent of the total study population.

As noted above, a letter-questionnaire was sent to the physicians of cases giving authorization to submit medical data. Of the 212 cases for whom satisfactory information was gathered, 178 gave usable authorization allowing us to gather information from physicians. The remaining cases either did not give authorization or the name or address of the physician was insufficient for mailing. The 178 letter-questionnaires sent to physicians brought 163 replies, a response of about 90 per cent for the mailings, or 65 per cent as based on total cases. Only three were not usable for such reasons as no record of patient or not examined for cardiovascular disease. In addition, verification for 12 persons was received in other ways, such as by review of hospital records and through death certificates. Table 4 summarizes the information received from patients, physicians, and other sources.

Table 4—Response, Authorization and Physician Verification of Coronary Heart Disease Cases Reported by California Health Survey

		Male				Female			
			Calif. Health Survey Diagnosis Code				Calif. Health Survey Diagnosis Code		
	Total	Total	420.0	420.1	420.2	Total	420.0	420.1	420.2
Response to special health inquiry									
Total	250	150	19	108	23	100	31	41	28
Total response	212	126	16	89	21	86	30	34	22
By mail	114	78	8	60	10	36	9	15	12
By interview	98	48	8	29	11	50	21	19	10
Nonresponse	38	24	3	19	2	14	1	7	6
Authorization to physician									
Total	212	126	16	89	21	86	30	34	22
Authorization given	179	110	12	81	17	69	25	26	18
Authorization not given	33	16	4	8	4	17	5	8	4
Letters to physicians									
Total	179	110	12	81	17	69	25	26	18
Sent	178	109	11	81	17	69	25	26	18
Not sent (insufficient address, etc.)	1	1	1	—	—	—	—	—	—
Response by physicians									
Total	178	109	11	81	17	69	25	26	18
Satisfactory reply	163	98	10	74	14	65	24	24	17
Unsatisfactory reply	3	2	—	2	—	1	1	—	—
No reply	12	9	1	5	3	3	—	2	1
Diagnoses									
Total	175	107	12	79	16	68	26	25	17
By physician's reply	163	98	10	74	14	65	24	24	17
By other sources	12	9	2	5	2	3	2	1	—
Verification									
Total	175	107	12	79	16	68	26	25	17
No cardiovascular disease	16	6	4	2	—	10	5	2	3
Cardiovascular disease	159	101	8	77	16	58	21	23	14
Other CVD	19	4	1	3	—	15	10	4	1
Coronary heart disease	140	97	7	74	16	43	11	19	13
CHD only	118	86	7	66	13	32	10	13	9
CHD, with other CVD	22	11	—	8	3	11	1	6	4

Findings

The first objective of this study was verification of the conditions reported in the California Health Survey. Reported coronary heart disease in the California Health Survey was coded to the ISC codes "arteriosclerotic heart disease so described" (420.0), "heart disease specified as involving coronary arteries" (420.1), and "angina pectoris without mention of coronary disease" (420.2). The cases in these groups numbered 50, 149, and 51, respectively. Diagnostic information was obtained for 175 of the 250 cases with little difference by ISC code subgroups. Of these diagnoses, 163 were from physician replies and 12 from other sources.

Three comments may be made on the data presented in Tables 4 and 5.

The proportion of cases diagnosed as

Table 5—Basis of Diagnosis of Verified Coronary Heart

	Total		Male		Female	
	No.	Per cent of Total	No.	Per cent of Total	No.	Per cent of Total
Total with diagnoses	175	100	107	100	68	100
Verified not CHD	35	20	10	9	25	37
Verified CHD	140	80	97	91	43	63
		Of verified CHD 100		Of verified CHD 100		Of verified CHD 100
ECG	111	79	82	85	29	68
ECG+History	73	52	54	56	19	44
ECG+history+other findings	20	14	14	15	6	14
ECG only	15	11	11	11	4	9
ECG+other findings	3	2	3	3	—	—
History—no ECG	15	11	6	6	9	21
History only	13	9	5	5	8	19
History+other findings	2	2	1	1	1	2
Other only	1	1	—	—	1	2
Basis not stated or verified by death certificates	13	9	9	9	4	9

coronary heart disease differed according to the California Health Survey ISC subgroup. Only 18 of the 50 cases coded to arteriosclerotic heart disease (ISC 420.0) were diagnosed as coronary heart disease. Diagnosis as coronary was obtained for 93 of the 149 cases "specified coronary" (ISC 420.1) and for 29 of the 51 cases coded "angina" (ISC 420.2). If only those cases with a diagnosis are considered, 89 per cent of the specified coronary and 88 per cent of the angina cases were verified, but only 47 per cent of the arteriosclerotic heart disease cases.

A larger proportion of males than of females (71–45 per cent) were initially reported with heart disease involving the coronary arteries (ISC 420.1). Angina was coded more often than arteriosclerotic heart disease in both sexes. The diagnoses of male cases were more often verified than were the diagnoses of female cases. This higher verification rate applies to all three ISC groups and whether considered for total cases or for cases with verification. The proportion of women exceeded that of men in both nonconfirmed categories: "no cardiovascular disease" and "other cardiovascular disease." Coronary heart disease with other cardiovascular disease (often angina with hypertension) was reported more often in women than in men.

The physician was asked to give the basis for his diagnosis. Electrocardiographic findings, usually with other evidence, were mentioned in over three-fourths of the physician reports verifying coronary heart disease as the diagnosis. Electrocardiographic evidence and a characteristic history and course furnished the basis for diagnosis of 60

per cent of the cases. Here, too, sex differences were noted. Diagnoses with electrocardiographic findings were reported more frequently in men while diagnoses based on a history only were more frequent in women.

Examples of Etiological Findings

The reported coronary heart disease cases studied herein represent a minimal number and may not be representative of cases in the survey population. Furthermore, the cases studied so far are survivors and as such may not be representative of persons dying shortly after their first episode of disease. Hence, adequate presentation of case-control comparisons cannot be made at this time. However, for purposes of illustration, the raw data on several items are presented in Table 6 for males aged 35–64 years. Incorporated in the table are estimates of several categories of cases not yet investigated, together with the total prevalence estimate developed previously.

This table indicates the relative num-

Table 6—Estimates of Numbers of Cases in Various Categories and Illustrative Case-Control Comparisons for Category One Males, Aged 35–64

		Estimated Numbers			
One year prevalence	Total	187±			
Undiagnosable		16±			
Deaths in one year (category 3)					
Diagnosable	Total	171±			
Undiagnosed and unreported (categories 4 and 5)			52±		
Diagnosed	Total		119±		
Heart disease, unspecified (category 2)				31±	
Coronary heart disease (category 1)	Total			88	
Verified not coronary by physician reply					(5)*
No answer to questionnaire					14
Unverified, no physician report					14
Verified coronary by physician reply					60

Illustrative Comparisons

	Verified Coronary	Control	Unverified Coronary	Control
	60	60	14	14
Weight				
Ht. over cube root of wt. at age 35				
Heavy—under 11.9	5	3	3	2
Med. heavy—12.0–12.4	9	21	3	1
Med. light—12.5–12.9	18	23	4	8
Light—13.0 and over	25	12	4	2
No answer	3	1	—	1

(Cont.)

Table 6—Continued

Age at which reading glasses or bifocals were needed	Verified Coronary	Control	Unverified Coronary	Control
Less than 40	9	5	4	2
40–44	17	3	3	1
45–49	13	14	—	5
50–54	10	17	1	1
55 and over	7	12	1	1
No glasses	1	4	3	3
No answer	3	5	2	1
Statement of muscularity				
Much more muscular	7	4	2	—
Little more muscular	17	34	6	6
Little less muscular	33	19	5	6
Much less muscular	2	2	1	2
Average and no answer	1	1	—	—
Statement of temperament				
Much less nervous	3	13	—	2
Little less nervous	13	20	4	5
Little more nervous	33	21	8	6
Much more nervous	8	5	2	1
Average and no answer	3	1	—	—
Number of sports continued in adult life				
0	5	10	3	2
1	8	7	1	1
2	13	16	1	5
3	11	2	4	4
4 and over	15	16	2	1
No answer	8	9	3	1
Diet: grams of fat per day				
Under 50	13	8	1	2
50–59	13	11	4	3
60–69	10	13	2	1
70–79	7	6	1	—
80–89	3	7	2	2
90 and over	11	15	4	5
No answer	3	—	—	1
Cigarette smoking				
Nonsmoker	7	18	3	5
Smoker				
¼ pack per day	7	3	—	1
½ pack per day	5	10	2	1
1 pack per day	21	17	5	4
1½ pack per day	7	7	2	3
2 or + pack per day	10	3	2	—
Amount not stated	3	2	—	—
No answer	—	—	—	—
Income change since 1950				
No change, or no direction reported	10	15	3	7
Gone up	16	28	4	5
No answer	1	—	—	—
Gone down	33	17	7	2
Due to:				
Retirement and/or unemployment	8	9	1	—
Heart disease	19	1	2	—
Other illness	—	1	1	1
Other and no answer	6	6	3	1

* Excluded.

bers of the estimated total cases, the unstudied cases, and the study group and, thus, cautions against drawing any conclusions at this time. It does, however, show some of the variables being examined, and preliminary tabulations of the results being obtained.

Summary

The study plan and preliminary findings of an epidemiological investigation of coronary heart disease in the California Health Survey population, a representative sample of the population of California, are reported. Five possible categories of survey coronary heart disease cases are distinguished: (1) reported as such; (2) reported as heart disease, unspecified; (3) undiagnosed, but dying of coronary heart disease within the year following the survey; (4) diagnosed but unreported as coronary disease or heart disease, unspecified; and (5) diagnosable but undiagnosed, hence unreported. Estimates indicate that cases reported as coronary heart disease comprise about half the total, and that heart disease, unspecified, confirmed as coronary heart disease brings reported cases to about two-thirds of the total possible cases.

The first stage was a study of the 250 reported coronary heart disease cases, using a combination of mailed questionnaires and interviews. A response of 85 per cent was achieved. Over 90 per cent of the queried physicians gave diagnostic information. This, and other sources, verified 93 of the 106 specified coronary cases (ISC 420.1) and 29 of of 35 cases of angina (ISC 420.2). Less than half, 18 of 37, of the cases coded arteriosclerotic heart disease (420.0) were verified as coronary. More than half the diagnoses were based on the electrocardiogram and a history in combination, some by electrocardiogram alone, some by history alone. Some preliminary tables are presented, illustrating case-control comparisons on physique, temperament, dietary fat, and smoking history. Additional groups of coronary heart disease cases (categories 2 and 3) in this population are being identified and will be investigated.

ACKNOWLEDGMENTS—The study staff received valuable consultation in developing the questionnaire from the Nutrition Service and the Medical Social Service of the department, as well as from John J. Sampson, M.D., of San Francisco. Assistance in pretesting the questionnaire was provided by Malcolm S. M. Watts, M.D., chief of the staff of the Cardiovascular Case Progress Index, University of California Medical Center, San Francisco, and by Alfred Maffly, administrator, and others of the Herrick Memorial Hospital, Berkeley. The field interviews were conducted by Lila Karpf and Dorothy Potts of the department. Lastly the cooperation of the persons in the study group and their physicians in providing the desired information is gratefully acknowledged.

REFERENCES

1. Bernstein, Felix. Altersichtigkeit und Lebenserwartung. Forschungen und Fortschritte 8, 21:272-273, 1932.
2. Breslow, Lester, and Mooney, H. William. The California Morbidity Survey, A Progress Report. California Med. 84, 2:95-97 (Feb.), 1956.
3. Dawber, T. R.; Meadors, G. F.; and Moore, F. E. Epidemiological Approaches to Heart Disease: The Framingham Studies. A.J.P.H. 41:279-286 (Mar.), 1951.
4. James, George, and Hillebee, Henry E. Evaluation During the Development of a Public Health Program in Chronic Disease: The Albany Cardiovascular Health Center. Ibid. 45:140-150 (Feb.), 1955.
5. Miller, David C.; Stare, Fredrick J.; White, Paul Dudley; and Gordon, John E. The Community Problem in Coronary Heart Disease: A Challenge for Epidemiological Research. Am. J. M. Sc. 232, 3:329-359 (Sept.), 1956.
6. Phillips, Edward; Chapman, John M.; and Goerke, L. S. Relative Values of Techniques Used in Detection of Heart Disease. Am. Heart J. 45, 2:319-330 (Mar.), 1953.
7. Weinerman, Richard E.; Breslow, Lester; Belloc, Nedra; Waybur, Anne; and Millmore, Benno K. Multiphasic Screening of Longshoremen with Organized Medical Follow-up. A.J.P.H. 42, 12:1552-1567 (Dec.), 1952.

State of California
DEPARTMENT OF PUBLIC HEALTH

CONFIDENTIAL

SPECIAL HEALTH INQUIRY

PERSONAL DATA

Your name - last ____ first ____ middle ____

Your present street or rural address ____ City or town ____

Your birthplace - City or county ____ State or country ____ Your birthdate (mo., day, yr.) ____ Your age (in years) ____

Father's birthplace (state or country) ____ Mother's birthplace (state or country) ____

PHYSIQUE

How tall are you?	How much do you weigh now?	How much did you weigh five years ago?	How much did you weigh when you were 25?	How much did you weigh when you were 21?
____ Ft. ____ In.	____ Lbs.	____ Lbs.	____ Lbs.	____ Lbs.

Check one box in each line to describe your adult body build

Fatness, compared to the average:	☐ Much fatter	☐ A little fatter	☐ A little less fat	☐ Much less fat
Muscularity, compared to the average:	☐ Much more muscular	☐ A little more muscular	☐ A little less muscular	☐ Much less muscular
Thinness, compared to the average:	☐ Much thinner	☐ A little thinner	☐ A little less thin	☐ Much less thin

If you wear reading glasses, or bifocals, how old were you when you first needed them? ____

TEMPERAMENT

Compared with the average of all people, how nervous, tense, or aggressive would you consider yourself?

☐ Much less than average ☐ A little less than average ☐ A little more than average ☐ Much more than average

ACTIVITY OF WORK

What is your usual occupation, the one you have followed for most of your working life? (Answer even if not working now.)

Job title (What is your job called? Such as doctor, laborer, housewife, etc.) ____

Industry (What business is this job in?) ____ Employer (What company, government agency, or person do you work for?) ____

How much physical labor is there in this work compared with the average of all types of work? (Pushing, pulling, lifting, walking, etc.)

☐ Much less labor ☐ A little less labor ☐ A little more labor ☐ Much more labor

How much nervous strain is there in this work compared with the average of all types of work? (Worry, responsibility, decisions, conflict, etc.)

☐ Much less strain ☐ A little strain ☐ A little more strain ☐ Much more strain

In this work, how many hours per day do you spend:

Sitting: ____ hrs. Standing or walking: ____ hrs. Other activity, specify: ____ ____ hrs.

How many years have you worked at this occupation? ____ Years

Are you still working at this occupation? ☐ Yes ☐ No

If you are no longer working at this usual occupation:

When did you leave this occupation? ____

Why did you leave this occupation? ____

What are you doing now? ____

Use the space below to write a brief description of any other important occupations, how long you followed them, and your reasons for change: (Any additional comments you want to make can be entered here)

The information obtained in this survey will be accorded confidential treatment by the California Department of Public Health. Individual reports will be used for statistical purposes only, and will be seen only by authorized employees who are assigned to work on this project. Only statistical summaries will be published, and individual returns will not be used for purposes of regulation or administration of any program.

- 2 -

RECREATIONAL ACTIVITY

Did you attend high school? ☐ Yes ☐ No

If "yes", check (✓) the sports you participated in. (Double check (✓✓) any you won a letter in)
☐ Baseball ☐ Basketball ☐ Football ☐ Other(s), specify: _____ ☐ None

Did you attend a college or university? ☐ Yes ☐ No

If "yes", check (✓) the sports you participated in. (Double check (✓✓) any you won a letter in)
☐ Baseball ☐ Basketball ☐ Football ☐ Other(s), specify: _____ ☐ None

Check below any sports you kept up for at least five years after you left school:
☐ Baseball ☐ Hunting ☐ Golf ☐ Riding ☐ Skating ☐ None
☐ Fishing ☐ Tennis ☐ Swimming ☐ Bowling ☐ Other, specify: _____

What other regular physical activities, outside work, have you carried on through adult life?

Daily walking: ☐ Less than ¼ mile (6 blocks) ☐ ¼ to 1 mile ☐ 1 to 2 miles ☐ 2 miles or more

Daily work in house or garden: ☐ Less than ½ hour ☐ ½ to 1 hour ☐ 1 to 2 hours ☐ 2 hours or more

Other, specify: _____ Hours per day _____

FOOD HABITS

In the year 1950: How often did you eat the following foods? (If on a diet in 1950, before you went on a diet.)	Check one Answer on Each Line					
	3 Times a Day or More	Twice a Day	Once a Day	3 - 4 Times a Week	Once or Twice a Week	Less Than Once a Week or Never
Whole milk						
Cream						
Butter or margarine						
Cheese						
Eggs						
Bacon						
Pork or ham						
Fried foods						
Gravies						
Salad dressings						
Cream soups						
Pies, doughnuts, sweet rolls, etc.						
Ice cream, malts, milk shakes						
Chocolate, chocolate candy, cocoa						
Nuts						
Avocado						
Peanut butter						
Potato chips, corn chips, etc.						

How did you salt your food?
☐ Never added salt at table ☐ Added salt only after tasting ☐ Generally added salt before tasting

Are you now on a diet?
☐ Yes ☐ No If "yes", how long have you been on this diet? _____

If "yes", what kinds of food are not allowed on this diet?

_____

If "yes", are you on this diet because of doctor's orders? ☐ Yes ☐ No

FAMILY LONGEVITY

		Father	Mother	How many brothers and sisters do you have? ___ (Indicate age and sex below)			
If living, present age							
If deceased:	Age at death						
	Cause of death (if you know it)						

SMOKING HABITS

Have you ever smoked cigarettes regularly for at least one year? ☐ Yes ☐ No

If answer is yes, check the highest number of years you have smoked:
☐ One year or more, but less than 5
☐ Five years or more, but less than 10
☐ Ten years or more, but less than 20
☐ Twenty years or more

At present, how many cigarettes do you smoke? (If you have quit smoking, how many cigarettes did you smoke before you quit?)
☐ Less than 5 cigarettes per day
☐ About 1/2 package per day
☐ About 1 package per day
☐ About 1 1/2 packages per day
☐ About 2 packages (or more) per day

NOTE: The questions we ask below have been deliberately made general. We want them to be questions that can be answered by people who have various illnesses and by people who have no illness at all. Please answer these questions as they apply to yourself, whether or not you have any illness.

INCOME

Has your own personal income changed since 1950? ☐ Yes ☐ No

If "yes", in which way has it changed?
☐ Gone down a lot ☐ Gone down a little ☐ Gone up a little ☐ Gone up a lot

If "yes", what was the main reason for this change?
☐ General raise ☐ Unemployment ☐ Illness, what illness? _____
☐ Retirement ☐ Promotion ☐ Other, specify: _____

RESOURCES

If your income has gone down since 1950, check the resources you have used to make ends meet
☐ Company retirement ☐ Friends or relatives ☐ Selling property
☐ Old Age Assistance ☐ Savings and investments ☐ Other, specify: _____
☐ Social Security (OASI) ☐ Cut living standards

Any further comments:

EMPLOYMENT

If your income has gone down because of illness, have you looked for work? ☐ Yes ☐ No

If "yes", have you ever been refused a job because of illness? ☐ Yes ☐ No

Any further comments:

HOUSING

Have you moved from one house to another since 1950? ☐ Yes ☐ No

If "yes", what was your main reason for moving?
☐ To better house ☐ Unemployment ☐ Illness, what illness? _____
☐ Retirement ☐ Transfer ☐ Other, specify: _____

If you have moved due to illness, how did the illness force you to move?
☐ Reduced income ☐ No stair climbing ☐ Other, specify: _____
☐ Better climate ☐ Closer to medical care

Any further comments:

SOCIAL LIFE

Has your social activity changed since 1950? ☐ Yes ☐ No

If "yes", which way has it changed?
☐ Gone down a lot ☐ Gone down a little ☐ Gone up a little ☐ Gone up a lot

If "yes", what was the main reason for this change?
☐ Change in family ☐ Unemployment ☐ Illness, what illness? _____
☐ Retirement ☐ Moved to new town ☐ Other, specify: _____

Any further comments:

STATUS

Do you think that people feel the same way about you as they did in 1950? ☐ Yes ☐ No

If "no", what was the main reason for this change?
☐ Retirement ☐ Unemployment ☐ Just age ☐ Illness, what illness? _____
☐ Other, specify: _____

Any further comments:

OTHER IMPORTANT WAYS

In what other important ways has life changed for you since 1950? (Please write here, also, any additional comments you may have on the previous questions.)

CONFIDENTIAL

4

	Have you had any of the following conditions?	Yes	No	What did the doctor say it was? Did he use any medical terms?	Year Condition Began	Doctor's Name and Address (City or Town, State)
PHYSICAL CONDITIONS	Chronic bronchitis					
	Hardening of arteries					
	High blood pressure					
	Heart trouble					
	Arthritis or rheumatism					
	Stomach ulcer					
	Thyroid disease					
	Kidney trouble					
	Diabetes					
	Gout					
	Any other chronic conditions?					

AUTHORIZATION

We need to have more information on the exact medical facts about these conditions. This will enable us to study these medical facts along with the other facts you have given us. Will you give your doctor(s) permission to give us details on your conditions? ☐ Yes ☐ No

To: Physicians whose names are furnished by me to the California State Department of Public Health

You are hereby authorized to give to the California Department of Public Health such medical or surgical information as they may request pertaining to my current and past illnesses.

Signature _____ _____, 1956
Month Day

The information obtained in this survey will be accorded confidential treatment by the California Department of Public Health. Individual reports will be used for statistical purposes only, and will be seen only by authorized employees who are assigned to work on this project. Only statistical summaries will be published, and individual returns will not be used for purposes of regulation or administration of any program.

Discussion

Implications to the Biostatistician

ANTONIO CIOCCO, D.Sc., F.A.P.H.A.

At last we have some figures on the incidence as well as on the prevalence of coronary heart disease. The data summarized here show that we are keeping to the concept which was formulated some years ago by Frost, the concept that the first step in the study of chronic illnesses should include "systematic collective observations on the incidence of . . . diseases. . . ." Three of the four papers presented here furnish data based on such observations.

The rates computed from these data apparently indicate that the incidence of coronary heart disease was different in the three groups under observation. Differences such as those shown provide the meat and drink on which are nourished studies, and ideas for studies, on the factors related to the incidence of heart disease or any other disease. When differences are found, the investigator, and the statistician in particular, considers it his first order of business to determine their meaning in terms of differences in the composition of the groups with respect to age, occupation, or other traits; in terms of sampling variation, etc. Tests of significance, estimation technics, calculation of specific and adjusted rates, and other procedures with which you are familiar are the means whereby we assess the meaning of the differences and judge the value of exploring further the relationships of selected variables to the incidence rates. However, before we employ these established procedures, consideration should be given to the need to solve a basic problem regarding the calculation of the incidence rate itself. This problem arises whenever we are dealing with long-term studies.

As we know, the incidence rate is calculated in order to estimate the probability of acquiring a disease in an interval of time. (By definition, the incidence rate is the ratio of the number of persons who acquire the disease within a certain interval of time to the number of persons in the specified population group who are free of the disease at the beginning of the interval and are exposed to the risk of acquiring it.) In dealing with a chronic disease the problem is that of choosing the proper numbers for the numerator and the denominator of the rate in view of the complex situation which develops when a closed population is maintained under observation for a long period of time.

The data of the three studies reported here illustrate the complexity of this situation. A sample is selected for study, and then a certain proportion of the persons in the sample refuses to participate. Among the persons kept under observation for a stated period of time, some refuse to participate further; some move away; some die from coronary heart disease; some die from other heart diseases; some die from other causes. Among the persons kept under observation who survive to the end of the interval of observation, some demonstrate coronary heart disease; some have other forms of heart disease;

Dr. Ciocco is with the Department of Biostatistics, University of Pittsburgh Graduate School of Public Health, Pittsburgh, Pa.

some have other disease conditions; and some are presumably negative. Which of these numbers or combination of numbers should be included in the numerator and denominator of the incidence rate? When we use as numerator the number of persons who have developed coronary heart disease or have died from it, and as denominator the number of persons first placed under observation, we are assuming that the persons lost through refusal, migration, death from other causes, and the persons who develop other forms of heart diseases and other sicknesses have not developed coronary heart disease. To the extent that this assumption is incorrect we shall be underestimating the incidence rate.

If we compute the incidence rate by putting in the numerator those persons known to have acquired coronary heart disease or died from it, and in the denominator only those who have survived to the end of the period of observation, we are assuming that coronary heart disease occurs among those who have been omitted at the same rate as in those who have been included. To the extent that this assumption errs we shall overestimate or underestimate the incidence rate depending upon the occurrence of coronary heart disease among those omitted.

As these long-term studies extend in time, these errors will be compounded, and may become larger because mortality and perhaps even refusal rates with time will increase. Under these circumstances, after a number of years, we cannot be too sure that we know to what universe the findings can be generalized because the original sampling scheme will have been confused. Calculations of sampling errors, adjustments for age, etc., has little meaning when the magnitude of the error of the rate itself is unknown.

Many of you are well aware of this problem. All long-term studies conducted to date, including those with which I have been associated and those discussed here, have been faced with this problem. Beginning with the classical studies of Frost on tuberculosis, attempts have been made to solve it, but no one has yet presented a solution based on sound theoretical foundations that is generally applicable to the determination of the incidence of diseases such as coronary heart disease.

In brief, we have yet to develop analytical procedures for long-term studies that will allow us to make adjustments for possible interactions between the incidence of the disease condition on the one hand and refusals, migration, and morbidity and mortality from other disease conditions on the other; and thus allow us to estimate the true incidence of a disease condition.

The development of such procedures is the task which the statistician faces, and in my opinion is the most significant implication of the studies reported here. Until this development is accomplished, comparisons of incidence rates from place to place or interpretations of relationships between incidence rate and possible etiological factors have to be accepted with several grains of salt.

From the time that we first became aware of the importance of chronic diseases to public health we have literally begged for the development of long-term studies. Through the efforts of groups as are here represented, such studies on coronary heart disease have become a reality. It is time, therefore, that we develop appropriate analytical tools to extract from these studies their real meaning.

Discussion

Implications to the Nutritionist

NEVIN S. SCRIMSHAW, M.D., F.A.P.H.A.

I appreciate the opportunity to comment specifically on the nutritional implications of the epidemiological studies of coronary heart disease conducted in four areas of the United States and presented at this symposium.

Dr. Paul White in his opening remarks stressed the importance of the epidemiological approach to coronary heart disease and gave some examples of the way in which epidemiological comparisons can furnish evidence for the role of a number of potential factors. You will note that he stressed the importance of world-wide studies of the frequency of this type of heart disease in populations with widely different ways of life, including varied dietary habits.

Our United States population in diet and even in activity, stress, and certain other factors of possible importance is remarkably homogeneous in comparison with the total range of human living conditions in our contemporary world. Dr. White also pointed out the major service which Dr. Ancel Keys has done in emphasizing for a number of years that the real clues to the solution of the coronary heart disease problems are likely to come from studying the different frequency of the disease and its manifestations in populations that differ in their modes of life. Obesity is perhaps an exception in that it can be studied within the United States samples, but it can be shown statistically that eliminating all obesity would effect only a relatively small proportion of the total problem of coronary heart disease in the United States.

From the point of view of the nutritionist, therefore, much of the value of the epidemiological studies that have been described this afternoon will come when they are compared with similar studies elsewhere.

Perhaps I am particularly conscious of this because I am working in an area, Central America, in which the majority of the people are essentially free of coronary heart disease (an immunity unfortunately not shared by either United States consultants or the more privileged local groups—physicians, lawyers, and other business and professional persons). For some time I, too, suspected that inadequate statistics might explain much of the reported lower incidence of coronary heart disease in many so-called "under-developed areas." However, as Dr. Francisco Grande reviewed this morning, there is now sufficient proof that many of the differences are real.

A convincing example is the recent work of Dr. Carlos Tejada, pathologist of the Institute of Nutrition of Central America and Panama, together with Dr. Ira Gore, pathologist of the Department of Nutrition of the Harvard School of Public Health.[1] They were able to examine within a single month, approximately 600 aortas accumulated from persons dying in New Orleans Charity Hospital, 300 dying in the General Hospital in Guatemala and, therefore, belonging to the low income group.

Dr. Scrimshaw is with the Institute of Nutrition of Central America and Panama, Guatemala City, Guatemala.

The differences between the Central Americans and North Americans were spectacular.

Every type of aortic atherosclerotic lesion began earlier and subsequently involved a more extensive area at each decade of age in the New Orleans material. Hemorrhagic, ulcerated, necrotic and calcified lesions began to be present to a significant degree after age 30 and increased rapidly after age 40 in the New Orleans aortas. In the Guatemalan ones, they did not begin until age 50 and increased moderately after age 60. In other words, the people of New Orleans acquired a given degree of surface involvement with severe aortic lesions at least 20 years of age earlier than the Guatemalans.

While these data refer only to aortic lesions, it is striking that there were 51 cases of myocardial infarction in the New Orleans study group and only one in the Guatemalans included in the study.

I should add that racial differences do not serve to explain the findings since they appear grossly similar in more than 200 Costa Rican aortas that are now under study. Although the Guatemalan population is partially Mayan Indian in origin, the Costa Rican people by history, appearance and major blood group distribution are of European ancestry.

When one sees results like these, the conclusion is inescapable that environmental factors are responsible for differences, such as these between lower income Central Americans and the general population in the United States, and almost certainly the factor or factors when identified fully will prove to be largely within our control.

The major dietary differences lie in the amount and kinds of fat and protein. The Central Americans were receiving an average of not more than 15 per cent in their diets; the persons in New Orleans were probably consuming closer to 40 per cent of their calories from this source. The Central Americans also consumed much more vegetable and less animal protein and were more active physically. Their caloric intake may in some cases have been slightly higher but they were decidedly leaner. (Whether they were under any less psychological stress is highly debatable.) The point which I wish to emphasize is that a careful comparison of both the epidemiology of coronary heart disease and the prevalent environmental influences in two such different populations should be most fruitful.

A study appeared recently in the Journal of Nutrition which illustrates the fallacy of drawing sweeping negative conclusions from the study of a single group with small internal variations in the factors analyzed.[2] The variable happened to be serum cholesterol and not coronary heart disease, but the principle demonstrated would be the same in either case. The authors concluded that neither fat nor protein in the diet had any influence on serum cholesterol in women. However, the cholesterol groups began at 160 mg per cent; the percentage of calories from fat within these groups ranged only from 37.5 to 43 per cent and the variation in protein was even less. With a standard deviation for percentage of calories from fat of 5 per cent, it is unlikely that a single person in their study group even approached the mean percentage of calories from fat of 8 per cent encountered in rural Guatemala or for that matter had serum cholesterol values approximating the mean value of 130 mg per cent for rural Guatemalan males age 20 to 29.[3] How much more useful their data are for comparison with groups in other areas with the 8 per cent or even 15 or 20 per cent of calories from fat, for there are many such groups in the world. Certainly their conclusions, while statistically valid within their sample, have no meaning in terms of the basic question—does serum cholesterol vary with dietary fat within

the range of the common human diet?

When we examine the nutritional implications of epidemiological studies of coronary heart disease in widely differing areas, there are reasonable grounds for believing dietary factors to be of major importance. To go further than this is to enter into controversy. Certainly there is increasing evidence to suggest that fat is involved, but as a recent editorial in Lancet [4] warns: "Noxious processes must persist for long periods before overt disease is manifest. In this type of research the unit of time is the decade." Moreover, there are a number of apparent exceptions to the fat hypothesis. It is true that ones such as the often maligned Eskimos and the relatively low incidence in the populations of Scandinavia are being explained by better epidemiological data or by the increasing attention given to the kind as well as the amount of fat. Not all of the apparent exceptions, however, have as yet been satisfactorily explained.

The work on the relative influence of unsaturated dietary fat, or at least fat relatively rich in essential fatty acids, was ably reviewed and discussed in the Food and Nutrition Section session this morning. Certainly, the work in Canada so impressively presented by Dr. J. M. R. Beveridge this morning together with that of Ahrens in New York, Kinsell in California, and Bronte-Stewart in South Africa shows that the kind of fat does influence serum cholesterol in relatively short-term experiments. But there is no positive assurance as yet as to the long-term results which would be obtained from such studies. Obviously, there are few direct nutritional implications in the studies presented this afternoon unless they are interpreted in the light of the world picture.

In general, because of the great interest which has been aroused in the problem of diet in relation to atherosclerosis and the far-reaching repercussions which premature pronouncements might engender, the public health profession must use great care in evaluating the available data. A year ago, the World Health Organization convened in Geneva a study group on atherosclerosis composed of nearly two dozen experienced workers in various aspects of the problem from a number of countries. I believe that the conclusion of this group must still guide us today—namely, that there is not yet sufficient information or agreement on its interpretation on which to base public health programs aimed at the prevention of ischemic heart disease. The group, of course, agreed that obesity per se was undesirable, whether or not it influenced coronary heart disease, and there are other recommendations which we may wish to follow as individuals or even prescribe to patients, but we certainly cannot at this time embark with confidence on an attempt to bring about mass changes in food habits.

There is, however, every reason to believe that epidemiological studies of the type presented this afternoon, especially when carried out in many parts of the world will make possible definitive answers in a few years. It is then probable that we will have a double problem of application, one of bringing about desirable changes in the habits of more privileged groups and protecting those less privileged from changes which will increase their risk of coronary heart disease.

REFERENCES

1. Tejada, C., and Gore, I. Comparison of Atherosclerosis in Guatemala City and New Orleans. (To be published.)
2. Butler, L. C.; Childs, M. T.; and Forsythe, A. J. The Relation of Serum Cholesterol to the Physical Measurements and Diet of Women. J. Nutrition 59: 469-479 (Aug.), 1956.
3. Mann, G. V.; Munoz, J. A.; and Scrimshaw, N. S. The Serum Lipoprotein and Cholesterol Concentrations of Central and North Americans with Different Dietary Habits. Am. J. Med. 19:25-32 (July), 1955.
4. Fats and Disease (Leading Article). Lancet 1:547-553 (Apr.), 1956.

Summary

JAMES WATT, M.D., F.A.P.H.A.

I would like first to present a reverse twist to Dr. White's presentation and say that the epidemiologist needs to turn to the cardiologist. I say this because the major problems in the study of the epidemiology of coronary disease today are numerator problems, as was amply demonstrated by the other four papers on this panel. It is now impossible to get a definition of coronary artery disease which permits a clear separation between those with the disease and those without. Here the epidemiologist clearly needs the help of the clinical and laboratory cardiologists.

However, the four papers did show that application of the methodology we now have to population groups in Los Angeles, Calif., Albany, N. Y., and Framingham, Mass., has come up with fairly consistent and uniform prevalence and incidence rates of overt coronary disease in those age groups which can be compared. It may be that this methodology which, in its present state, does not clearly separate all the diseased from the well is reproducible enough that it can be used as a tool to produce an index of coronary disease in populations. Such an index could be used to study populations which differ by those characteristics thought to influence the occurrence of this disease.

These studies reported today undoubtedly will show and verify that certain characteristics of a population are associated with an increased incidence of coronary heart disease. Analysis of multiple characteristics, along the lines that were reported from the Framingham study, will, I think, eventually make it possible to accurately characterize a population in which susceptibility to coronary disease is very high. By the same token, highly resistant populations may be delineated.

Finally, I would like to draw your attention to the fact that three of the four studies reported on today were carried out by state and local health departments. This was expected since health departments, by their very nature, collect, analyze, and put to use information on health and disease. They are the logical sites for building population studies. I think we will see many other health departments embarking upon epidemiological studies of coronary disease, or for that matter all the chronic diseases, in the near future. I hope that this program has encouraged such an embarkation.

Dr. Watt is with the National Heart Institute, National Institutes of Health, Public Health Service, Bethesda, Md.